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Centro Investigador en Economía y Gestión de la Salud

Doctoral thesis by publications.
Tesis doctoral por compendio de publicaciones

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What have we learned from the economic impact of the COVID-19 outbreak? Critical analysis of economic factors and recommendations for the future.

¿Qué hemos aprendido del impacto económico del brote de la COVID-19? Análisis crítico de factores económicos y recomendaciones para el futuro.

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Supervisor and tutor: David Vivas-Consuelo

Director y tutor: David Vivas-Consuelo

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Valencia, July 2021

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Autorización de tesis por compendio de publicaciones.

El Profesor Dr. David Vivas-Consuelo

CERTIFICA

Que la presente memoria: «What have we learned from the economic impact of the COVID-19 outbreak? Critical analysis of economic factors and recommendations for the future» resume el trabajo de investigación realizado, bajo su dirección, por D. Julio Emilio Marco Franco y constituye su Tesis para optar al título de Doctor por compendio de publicaciones, con mención internacional.

Y para que conste, en cumplimiento de la legislación vigente, firman el presente certificado en Valencia a 21 de mayo de 2021.

Fdo.: Prof. Dr. David Vivas Consuelo

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Publications

1/ Marco-Franco, Julio Emilio, Guadalajara-Olmeda, Natividad, González-de Julián, Silvia and Vivas-Consuelo, David. (2020). COVID-19 Healthcare Planning: Predicting Mortality and The Role of the Herd Immunity Barrier in the General Population.
Sustainability, *12*(13) [5288], 8–10. https://doi.org/10.3390/su12135228
Impact factor: 2.576.— Q2.

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2/ Marco-Franco, Julio Emilio, Pita-Barros, Pedro, Vivas-Orts, David, González-de Julián, Silvia and Vivas-Consuelo, David. (2021). COVID-19, fake news, and vaccines: Should regulation be implemented?
Int. J. Environ. Res. Public Health, *18*(2), 744, 1–11. https://doi.org/10.3390/ijerph18020744
Impact factor: 2.849.— Q2.

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3/ Marco-Franco, Julio Emilio, Pita-Barros, Pedro, González-de Julián, Silvia, Sabat Iryna and Vivas-Consuelo, David. (2021). Simplified mathematical modelling of uncertainty: cost-effectiveness of COVID-19 vaccines in Spain. *Mathematics*, 9, 566, 1–15.
https://doi.org/10.3390/math9050566
Impact factor: 1.747. – Q1.

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Congress Conferences

♦ Julio E. Marco-Franco & David Vivas-Consuelo. *Lessons After Covid-19. Advances in Science and Economics Through Remote Information and Communication Technologies.* (2021). Charles Institute of European Studies. 3rd International Conference on Social Entrepreneurship, Social Innovation and Business Research, (SESB-MARCH-2021). March 27–28, 2011. Barcelona, Vol. 04. https://cies.education/proceedings/Issue 42. ISBN**:** 978-969-683-698-8.

♦ Julio E. Marco-Franco & David Vivas-Consuelo (2021). *Nuevo enfoque en el doctorado internacional.* [*New focus on international doctorat*e].VI Virtual Congress International: Education in the 21st Century. Effects of COVID-19. 14–28 April. EUMED Congress. ISBN pending.

♦ Julio E. Marco-Franco & David Vivas-Consuelo (2021). V*acunación en edad escolar* [*Vaccination at school age*]. VI Virtual Congress International. Education in the 21st Century: Effects of COVID-19. 14–28 April. EUMED Congress Covid-19: ISBN pending.

Keywords

SARS-CoV-2. COVID-19**.** Coronavirus. Pandemic. Outbreak. Healthcare costs. Health Economy. Vaccination. Herd immunity. Case Fatality Rate. Infectious Fatality Rate. Fake news. Misinformation. Medical code of ethics. Governmental regulations. COVID-19 vaccination. Cost-effectiveness Analysis (CEA). Quality Adjusted Life Years (QALY). Incremental Cost Effectiveness Ratio (ICER). Utility ratio. Collective choice. Best Adjustment of Related Values (BARV). Economic modelling. Predictive Modelling. Mathematical forecast models.

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There are men that fight one day and are good, others fight one year, and they are better, and there are those who fight many years and are very good, but there are the ones who fight their whole lives, and those are the indispensable ones (Bertolt Brecht).

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DEDICATION

To my dearest younger brother and best friend, Javier Marco Franco MD, who lost the battle with COVID-19 on May 14, 2020, and to the rest of the health professionals who also fell by the wayside in the fight against the pandemic.

IN MEMORIAM

Sit tibi terra levis

◇◇

如果你要问什么时候会有瘟疫，我会说是冬天。有一个人关注到从猪年到鼠年的困难 ... 一个人关注湖广的灾难，然后蔓延到中国所有的省份 ...

If you ask when the plague will come, I would say about wintertime… one worries about the difficulty of crossing from the pig year [2019] to the rat year [2020] … One worries about the onset of disaster in Huguang which then spreads to all provinces across China (Liu Ji, Bowen, 14th Century).

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Also, many thanks to all those who have provided comments, criticisms, technical suggestions, or information, particularly to Jose Manuel Valverde, President of the Medical Association of the Balearic Islands and to Joan Plovins, both primary care physicians in Majorca, for their estimates of outpatient medical care related to COVID-19.

Finally, I wish also to express my sincere thanks to Mr. John Wright for his help in editing the English.

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Table of Contents

Relation of Acronyms Used in this Text

5G	Fifth generation of cellular networks.
aaCFR	Age-adjusted Case Fatality Ratio.
BARV	Best Adjustment of Related Values.
BOE	Spanish Official Gazette.
Case-mix	Cohort of statistically related patients.
CCAA	Comunidades Autónomas [Spanish regions with certain autonomy].
CFR	Case Fatality Rate.
CIS	Centro de Investigaciones Sociológicas [Spanish Soc. Res.].
CMBD	Conjunto Mínimo Básico de Datos [Minimum Basic data set].
ECB	European Central Bank.
EMA	European Medicines Agency.
EU	European Union.
FN	Fake news.
GDP	Gross Domestic Product.
HIS	Hospital Information System.
ICD9CM	International Classification of Diseases.
ICER	Incremental Cost-Effectiveness Ratio.
ICT	Information and Communication Technologies.
ICU	Intensive Care Unit.
IFR	Infection Fatality Rate.
INE	Instituto Nacional de Estadística [National Institute of Statistics].
MoMo	Mortality Monitoring System.
NHS	National Health Service (UK).
OP	Outpatient.
PCR	A test based on Polymerase Chain Reaction.
PMP	Per Million Population.
QALY	Quality-adjusted life-year.
*R*o	Basic reproductive ratio.
RNA Virus	A virus that has ribonucleic acid (RNA) as its genetic material.
Statista	Macro database.
WHO	World Health Organisation.

Summary

The SARS-CoV-2 Coronavirus outbreak has posed a challenge to the economy, social life, and health services. Just when information was most needed for economic planning, monitoring, and reporting services were unable, despite extraordinary efforts to provide consistent data, as government agencies themselves acknowledged.

This thesis includes three articles published during the COVID-19 outbreaks and additional research outside the publication set. The overall aim of the research is to provide information through alternative estimates. Several methodologies have been used, including mathematical models for epidemiological prediction, Best Adjustment of Related Values (BARV), analyses of different surveys and bibliometric methodology, taking advantage of or offering an alternative to, more complex options such as Bayesian methods, Monte Carlo simulations or Markov chains, although some data obtained are partially supported by these methodologies. Each article addresses a key issue related to the COVID-19 pandemic.

The first publication focuses on basic epidemiological data. It refers to the first outbreak of COVID-19, estimating its duration, incidence, prevalence, Infection Fatality Rate (IFR) and Case Fatality Rate (CFR). As a highlight of this work, the seroprevalence was anticipated to be too low for herd immunity to play a role. Although the value obtained was approximately 2% lower than that subsequently demonstrated by a population-based study (Instituto Carlos III), the conclusion on herd immunity remained unchanged, and the results confirmed the appropriateness of the approach.

The second publication focuses on legal issues and fake news, analysing reluctance to be vaccinated in the population, the impact of fake news on these behaviours, the legal possibilities of making vaccination mandatory, and possible actions against health professionals who publish fake news. The main conclusion was that, although a legal avenue could be found for mandatory vaccination and for governmental prosecution of fake news, public opinion seems to prefer that the authorities do not take the initiative, therefore it recommends promoting and encouraging public awareness.

The third publication presented a simplified mathematical model for estimating the cost-effectiveness of the COVID-19 vaccine. Data from two dates were obtained for the estimation of the direct costs to the health system due to COVID-19, computing the cost per citizen and per Gross Domestic Product (GDP), as well as the cost-effectiveness of the vaccine. The estimated incremental cost-effectiveness ratio (ICER) was calculated for two doses per person at a cost of 30 euros per dose (including administration). Assuming 70% effectiveness and with 70% of the population vaccinated, it was found to be 5,132 euros (4,926 – 5,276) per quality-adjusted life year (QALY) gained (as of 17 February 2021). The figure decreases with each day of the active pandemic.

Additional research not included in the set of articles focuses on human resources and education. It analyses the concerns of frontline staff, i.e., nurses, and how the pandemic has affected their scientific publications, as an index of the changes in the work climate experienced by this group. Through a comparative bibliometric study of publications in 2019 and 2020, the change in topics and fields was analysed, as a reflection of the impact of COVID-19 on nursing staff. It was found that in the fields of specialised care nursing and above all in primary care, the main problems detected are those related to protective measures and psychological factors, while the publications of nursing staff in nursing homes showed an increase in topics related to management and organisation.

Finally, some aspects of the implementation of telecommuting and distance learning have been reviewed. Some of the boosts in this field resulting from the pandemic could be very useful and remain in the future, such as the incorporation of teleworking for certain groups who cannot work face-to-face, or distance research, including doctoral programmes with an international mention.

In cases of crisis and uncertainty, health economics models and analyses allow data to be predicted with sufficient accuracy to be used by managers and planners.

Resumen

El brote de Coronavirus SARS-CoV-2 representó un reto para la economía, la vida social y los servicios sanitarios. Justo cuando más se necesitaba la información para la planificación económica, los servicios de vigilancia y notificación no fueron capaces de ofrecer, a pesar de esfuerzos extraordinarios, datos consistentes, como así reconocieron los propios organismos gubernamentales.

Esta tesis incluye tres artículos publicados durante los brotes de COVID-19 y una investigación adicional fuera del conjunto de publicaciones. La investigación tiene como objetivo general proporcionar información a través de estimaciones alternativas. Para ello se han utilizado varias metodologías, entre ellas los modelos matemáticos de predicción epidemiológica, el Mejor Ajuste de Valores Relacionados (BARV), los análisis de diferentes encuestas y la metodología bibliométrica, aprovechando u ofreciendo alternativas a los métodos bayesianos más complejos, las simulaciones de Monte Carlo o las cadenas de Markov, aunque algunos datos obtenidos se apoyan parcialmente en estas metodologías. Cada artículo aborda un tema esencial relacionado con la pandemia COVID-19.

La primera publicación se centra en los datos epidemiológicos básicos. Se refiere al primer brote de COVID-19, estimando su duración, incidencia, prevalencia, tasa de fallecimientos sobre infectados (IFR) y tasa de fallecimientos sobre casos (confirmados) (CFR). Como dato destacado de este trabajo, se previó que la seroprevalencia era demasiado baja para que la inmunidad de rebaño desempeñara algún papel. Aunque el valor obtenido fue aproximadamente un 2% inferior al que demostró posteriormente un estudio poblacional (Instituto Carlos III), la conclusión sobre la inmunidad de rebaño no cambió, y los resultados confirmaron la idoneidad del enfoque.

La segunda publicación se centró en las cuestiones legales y las noticias falsas, analizando la reticencia de la población a vacunarse, el impacto de las falsas noticas en estos comportamientos, las posibilidades legales de hacer obligatoria la vacuna y las posibles acciones contra los profesionales de la salud que publican noticias falsas. La principal conclusión fue que, aunque se podría encontrar una vía legal para la obligatoriedad de la vacunación, y para la persecución gubernamental de las noticias falsas, la opinión ciudadana parece preferir que la administración no tome la iniciativa, por lo que se recomienda promover y fomentar la concienciación ciudadana.

La tercera publicación presentó un modelo matemático simplificado para la estimación del coste-efectividad de la vacuna contra la COVID-19. Se actualizan los datos de dos fechas para la estimación de los costes directos para el sistema sanitario debidos a la COVID-19, computando el coste por ciudadano y por Producto Interior Bruto (PIB), así como el coste-efectividad de la vacuna. La estimó razón de coste-efectividad incremental (RCEI) para dos dosis por persona a un coste de 30 euros cada dosis (incluida la administración). Asumiendo al 70% de efectividad y con el 70% de la población vacunada resultó ser de 5.132 euros (4.926 – 5.276) por año de vida ajustado a calidad (AVAC) ganado (a 17 de febrero de 2021). Una cifra que desciende cada día de pandemia activa.

Se incluyó una investigación adicional, no incorporada en el conjunto de artículos, centrada en los recursos humanos y la educación. Se analizaron los temas preocupan al personal de primera línea, es decir, a la enfermería, y cómo la pandemia ha afectado a sus publicaciones científicas, como índice de los cambios en el clima laboral que sufre este colectivo. Mediante

un estudio bibliométrico comparativo entre las publicaciones de 2019 y 2020, se analizó el cambio de temas y ámbitos como reflejo del impacto del COVID-19 en el personal de enfermería. Así se comprobó que, en los ámbitos de enfermería de atención especializada, y sobre todo en atención primaria, los principales problemas detectados son los relacionados con las medidas de protección y los factores psicológicos mientras en las publicaciones del personal de enfermería de centros residenciales mostraron un incremento de los temas relacionados con la gestión y organización.

Finalmente se han revisado algunos aspectos de la implantación del teletrabajo y la educación a distancia. Algunos de los impulsos en este campo resultantes de la pandemia podrían ser de gran utilidad y permanecer en el futuro, como la incorporación del teletrabajo para determinados colectivos que no pueden trabajar de forma presencial, o la investigación a distancia incluyendo programas de doctorado con mención internacional.

En casos de crisis e incertidumbre, los modelos y análisis de la economía sanitaria permiten prever los datos con la suficiente exactitud como para ser utilizados por gestores y planificadores.

Resum

El brot de Coronavirus SARS-CoV-2 va representar un repte per a l'economia, la vida social i els serveis sanitaris. Quan més es necessitava la informació per a la planificació econòmica, malgrat esforços extraordinaris, els serveis de vigilància i notificació no van ser capaços d'oferir dades consistents, com així van reconèixer els mateixos organismes governamentals.
Aquesta tesi inclou tres articles publicats durant els brots de COVID-19 i una investigació addicional fora del conjunt de publicacions. La investigació té com a objectiu general proporcionar informació a través d'estimacions alternatives. Per a això s'han utilitzat diverses metodologies, entre elles els models matemàtics de predicció epidemiològica, el Millor Ajust de Valors Relacionats (BARV), les anàlisis de diferents enquestes i la metodologia bibliomètrica, aprofitant o oferint opcions alternatives als mètodes bayesians més complexos, les simulacions de Montecarlo o les cadenes de Markov, tot i que algunes dades obtingudes es recolzen parcialment en aquestes metodologies. Cada article aborda un tema essencial relacionat amb la pandèmia COVID-19.
La primera publicació se centra en les dades epidemiològiques bàsiques. Es refereix al primer brot de COVID-19, calculant la seua durada, incidència, prevalença, taxa de defuncions sobre infectats (IFR) i taxa de defuncions sobre casos (confirmats) (CFR). Com a dada destacada d'aquest treball, es va preveure que la seroprevalença era massa baixa perquè la immunitat de ramat exercirà algun paper. Tot i que el valor obtingut va ser aproximadament un 2% inferior al demostrat posteriorment en un estudi poblacional (Institut Carles III), la conclusió sobre la immunitat de ramat no va canviar, i els resultats van confirmar la idoneïtat de l'enfocament.
La segona publicació es va centrar en les qüestions legals i les notícies falses, analitzant la reticència de la població a vacunar-se, l'impacte de les falses notícies en aquests comportaments, les possibilitats legals de fer obligatòria la vacuna i les possibles accions contra els professionals de la salut que publiquen notícies falses. La principal conclusió va ser que, tot i que es podria trobar una via legal per l'obligatorietat de la vacunació, i per la persecució governamental de les notícies falses, l'opinió ciutadana sembla preferir que l'administració no prenga la iniciativa, per la qual cosa es recomana promoure i fomentar la conscienciació ciutadana.
La tercera publicació va presentar un model matemàtic simplificat per a l'estimació del cost-efectivitat de la vacuna contra la COVID-19. S'actualitzen les dades de dues dates per a l'estimació dels costos directes per al sistema sanitari deguts a la COVID-19, computant el cost per ciutadà i per Producte Interior Brut (PIB), així com el cost-efectivitat de la vacuna. La va estimar raó de cost-efectivitat incremental (RCEI) per dues dosis per persona a un cost de 30 euros cada dosi (inclosa l'administració). Assumint al 70% d'efectivitat i amb el 70% de la població vacunada va resultar ser de 5.132 euros (4.926 – 5.276) per any de vida ajustat a qualitat (AVAQ) (a 17 de febrer de 2021). Una xifra que descendeix cada dia de pandèmia activa.
Es va afegir una investigació addicional, no inclosa en el conjunt d'articles, centrada en els recursos humans i l'educació. Es van analitzar els temes que preocupen al personal de primera línia, és a dir, a la infermeria, i com la pandèmia ha afectat les seues publicacions científiques, com a índex dels canvis en el clima laboral que pateix aquest col·lectiu. Mitjançant un estudi bibliomètric comparatiu entre les publicacions de 2019 i 2020, es va analitzar el canvi de temes i camps com a reflex de l'impacte del COVID-19 en el personal d'infermeria. Així es va comprovar que en els àmbits d'infermeria d'atenció especialitzada, i sobretot en atenció primària, els principals problemes detectats són els relacionats amb les mesures de protecció

i els factors psicològics mentre en les publicacions del personal d'infermeria de centres residencials van mostrar un increment dels temes relacionats amb la gestió i organització.
Finalment s'han revisat alguns aspectes de la implantació del teletreball i l'educació a distància. Alguns dels impulsos en aquest camp resultants de la pandèmia podrien ser de gran utilitat i romandre en el futur, com la incorporació del teletreball per a determinats col·lectius que no poden treballar de forma presencial, o la investigació a distància incloent programes de doctorat amb menció internacional.
En casos de crisi i incertesa, els models i anàlisi de l'economia sanitària permeten preveure les dades amb la suficient exactitud per a ser utilitzats per gestors i planificadors.

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Preface

The unfortunate death of the doctoral candidate's younger brother led to a series of contacts with management professionals in Valencia where he worked, including the supervisor of this thesis, Professor Dr David Vivas Consuelo.

As a result of this interaction, the possibility of conducting a thesis on COVID-19 in his memory was raised. From the very beginning we were aware that the project had to be planned in a very different way from a conventional thesis

Firstly, because the COVID-19 issue was raising a lot of expectation with constant publications from multidisciplinary teams and prestigious institutions such as the Imperial College London or the CDC (Center for Disease Control and Prevention in the USA) counting on huge organization, funding, and personnel.

Secondly, the speed of publications would make a conventional thesis out of date long before it was published. Bear in mind that at the time of writing these lines, the web contains 1.5 billion publications with the word COVID. It was therefore necessary to opt for the thesis-by-publication format.

Thirdly, even for the article option, it was necessary to find publishers who would publish quickly and in open format. The mere one-week delay of the third article in the series meant that the data and tables had to be completely rethought.

Achieving the publications needed to meet the academic requirement, with the required quality and at that rate of scientific production, has represented a strenuous effort, with countless hours of work on a 7/7 workday schedule.

The plan of work had to be adapted to the tremendous dynamics of the COVID-19 research, including the addition of an article on vaccination, which became available much earlier than expected, creating enormous initial misgivings and a relentless flow of fake news.

A general strategy has been followed, adapted to the possibilities of mainly individual work, in an expanding area of studies by well-equipped multidisciplinary teams of experts: that is, the search for estimated results, sufficiently approximate to be used in health management, where precise adjustment is rarely necessary, but where early orientation of the expected order of magnitude is of enormous help in allocating human, material and economic resources appropriately.

The repeated experience in several countries (and even regions within the same territory) of incomplete, inaccurate or sometimes totally inconsistent data, resulting from a system that was overwhelmed and incapable of rigorous case tracking, led to the second strategy: obtaining information from the most reliable indirect sources, based on estimates of other data, through the Best Adjustment of Related Values (BARV) system, using a methodology similar to meta-analyses, seeking estimated values of related parameters that minimise the errors in the data in relation to those published in various series.

The general approach followed here was that, if official sources are overwhelmed, it does not make sense to overburden staff with additional sampling when they cannot adequately meet the main request. This principle has entailed that the analysis of the work climate presented

in the text, which has not, as of the moment of writing, been published as an article, was carried out by means of a computerised bibliometric study.

In all cases, the application of readily available methodology has been sought, and the mathematical functions and computer resources that have been used have been selected so that they would be available in most centres, not only in those countries with the greatest economic resources.
Many issues relating to COVID-19 are susceptible to political debate, but this paper will not enter in those issues, nor analyse aspects not within its scope. It proposes an outline of different analyses to draw lessons in five key areas:

In the face of inconsistent epidemiological data, how can we estimate the data now and in the future, if a similar situation were to recur?	Paper 1

Faced with a population wary of vaccines and amid a spread of fake news, is it possible to establish a regulation to make vaccination mandatory and to control fake news?	Paper 2

Is it possible to obtain an estimate of the cost of the pandemic and the benefit of vaccination?	Paper 3 Two International Congress Conferences

Is there any way to semi-quantitatively estimate the effects of COVID-19 on frontline staff?	Bibliometric work

Is there any benefit to be gained from the COVID-19 pandemic relating to education and telework?	Two International Congress Conferences

Julio Emilio Marco Franco
Porto, Portugal 20 May 2021.

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Chapter 1
Introduction

> COVID-19 is spreading human suffering worldwide; that is what we should all be focused on. But we are not doctors. We are economists – and COVID-19 is most definitely spreading economic suffering worldwide. The virus may in fact be as contagious economically as it is medically (Baldwin & Mauro, 2020)

Contagion was a film made in 2008 and released in 2011. It counted with the scientific advice of Columbia University professor Ian Lipkin who declared to HARDtalk's Stephen Sackur: «It is ironic. The reason we made this film was in fact to prevent something like this happening.»[1]

Instructive, and generally praised for its scientific accuracy, the film, directed by Steven Soderbergh, is about a highly deadly viral pandemic with respiratory symptoms, transmitted from bats and pigs in a slaughterhouse and originating in China. It shows the actions of the World Health Organization (WHO); the Centre for Infectious Disease Control and Prevention (CDC) in the United States; the installation of field hospitals in sports stadiums; the commercial interests and fights of pharmaceutical companies; the media, with the spread of fake news and conspiracy theories, including a denialist journalist with 12 million followers that pay his bail when he is arrested.

Further features of the film are; trackers; an explanation of the Basic Reproductive Ratio (R_o); the problems of burying the dead; hoarding by shoppers in supermarkets; the promotion of a drug based on a «miracle» plant; looting of shops and business; police quarantine checks; mass graves dug by the army; phrases such as «social distancing», «stay at home», «wash hands frequently» and comments such as «there are fifty states in this country with different systems and different protocols.»

The film also narrates the denialism towards information provided by the CDC and WHO accusing these of hiding data; social networks such as Facebook as a source of fakes; mutation of the virus; empty airports and gyms; curfews; and the long development period required for new vaccines (note that the movie was criticised because it presented a new vaccine produced in a «scientifically impossible short» [months] period of time). When the vaccine is achieved, shortages appear, along with the question of who gets vaccinated first; the guarded transport of vaccines; refusals to get blood drawn; vaccines by lottery of date of birth; vaccine depots at negative temperatures; teenagers angry by confinement, no handshaking...etc.

A single film production, with the principal assistance of one scholar, was able to foresee something that has surprised and baffled a myriad of experts from the world's leading public

[1] *https://www.bbc.com/news/av/entertainment-arts-53063584 (accessed on 15 December 2021).*

health organisations. While it was stated in the preface that this dissertation will not enter into political debate, it may be worth considering if as a society we really were prepared for a pandemic (this or another) and if society has reacted properly to the challenge.

This is not intended to be a critical commentary, but an aseptic description of a reality where lack of foresight has resulted in shortages of basic protective equipment such as masks and gloves, leading to avoidable morbidity and mortality, particularly among frontline and health workers. There have been several major errors, starting with the widespread misconception in society that there would never be a major future crisis in health or the economy.

Approaching this from a philosophical point of view, while it cannot be said that there have not been armed conflicts after the World War II (WWII), either as uprising, rebellion, insurgency, crisis, coups d'état, or open war (Korea, Vietnam, Congo, Indo-Pakistan, Algeria, Arab-Israeli, Iran-Iraq, Gulf, Afghanistan, Bosnia, etc.), in general they had a geographically limited extension and did not severely affect the peaceful life and progress of the majority of societies not involved in these conflicts and that for the last 75 years have experienced a linear progression of well-being —accompanied by an extraordinary growth of technologies, especially regarding information and communication (ICT)— and which it seems to have been assumed would continue to grow forever.

But nonlinearity is precisely a universal characteristic, from the movement of planets to water or life cycles, the characteristic nonlinearity of the world has been recorded in human's culture since the ancient Rigveda to the seven years period in the Genesis 41:20-30. It is present in the Maya calendar, in the ancient Greek and Roman philosophers, and in later ones (the eternal recurrence concept of Nietzsche) (Blaha, 2002).

As if that cyclical component inherent in life had never existed and the lessons learned from previous crises vanished —such as the disastrous effects of past epidemics, with high percentages of population deaths and economic ruin, as in the Plague Antonina (Byrne, 2010), or the social crisis at the end of the first millennium (although it must be recognized that there is controversy about the exact magnitude of these events)— this upward happy progression has been rocked by the COVID-19 pandemic, bringing the shadow of true lean times and generating health and economic insecurity, fear and confusion.

From the first moments of the first COVID-19 outbreak, it was clear that this was not just another epidemic. SARS-CoV-2 coronavirus spread rapidly and with a high mortality rate that not only affected the health economy but also extended to macro and micro economy in general throughout the planet. As Luis de Guindos vice-president of the European Central Bank (ECB) declared as early as April 2020 the situation was the most serious since the [2nd World] War (Perez, 2020).

Unlike other pandemics which originated in less economically dominant nations, COVID-19 has emerged in several of the largest economies in the world accounting for (as of March 5, 2020) 60 % of world supply and demand, 65% of manufacturing and 41% of exports (Baldwin & Mauro, 2020, p. 2).[2] Domestic demand became substantially affected as result of long-term shut down of the economy by public-health order and there was a break in the balance between supply and demand, with the consequent price adjustments (Balleer et al., 2020).

Stock markets and oil prices collapsed, and some sectors of the economy, such as tourism, suffered a double-digit decline, while for other products or services —such as hand sanitizer,

[2] A surprisingly early text on the pandemic, reinforcing the concept of speed of publication discussed in the preface. The authors really take this data from: World Bank World DataBank, FT COVID dashboard: *https://www.ft.com/content/a26fbf7e-48f8-11ea-aeb3-955839e06441 (accessed on 12 May 2020).*

e-commerce, virtual events, cyber security, home alarms, and home fitness, among others— there was a significant increase in demand (World Bank Group, 2020). Due to collective uncertainty and hysteria, some products disappeared from the stores in the early stages of the pandemic, notably in the example of toilet paper hoarding (Laato et al., 2020). Teaching procedures, labour efficacy and working patterns changed (Mayhew & Anand, 2020).

There were early forecasts about the economic situation and international responses from the International Monetary Fund (Gopinath, 2020), the World Bank (The World Bank, 2020), and many other organisations; a difficult job, as there was no previous information about viral pattern, nor knowledge of its future evolution, nor what the authorities would do in terms of quarantine, travelling or social restrictions and so on. It was a perfect storm for the inappropriateness of economic models, since they are usually based on the *ceteris paribus* consideration that only a few variables will change while assuming that those others not considered will not have a significant change or impact (Whitaker, 2011).

Spain has a network of epidemiologic monitoring, hospital information systems (HIS) and periodic statistical recording of information by the National Institute of Statistics (INE). In 1981 the European Minimum Basic data-set was approved for implementation by State members (Roger, 1981), in December 1987 the CMBD (Conjunto Mínimo Básico de datos), —a case-mix code system using coded using the International Classification of Diseases (ICD9CM)— began its development in Spain, becoming compulsory after 1992 (Sarria-Santamera, 2013). However, none of this could provide much help as it was a new virus with unknown epidemiological pattern and was collapsing the capacities of the system for proper recording. Initial plans became insufficient, and personal protection equipment shortage became critical as recognised by the WHO itself (World Health Organization, 2020a).

Inconsistencies of information become evident and recognised by the authorities themselves. So, amidst this situation or in case of not having sophisticated records of information, how to proceed? How can a health economist plan the resources needed, whether it will be necessary to expand the wards, buy new ventilators, or request emergency services, even those of the army in case of accumulation of corpses that exceed the usual capacity of funeral and cremation services?

The dissertation tries to draw some lessons from the pandemic. It analyses an alternative possibility for estimating needs using Best Adjustment of Related Values (BARV), and other simplified methods for crisis, available in the case of information systems breaking down, being overwhelmed, or in the case of less advanced register systems. It is based on estimations, since, although the better information the better health economy plan, it is not critical to know the figures to the decimal point. It also had the general goal of obtaining data without asking for additional surveys or asking for data forms to be filled in by staff who are working at the limit of their human possibilities.

The aim underling all the project is how to learn from the COVID-19 pandemic and how to figure out, with a reasonably close approach, values that are needed both for the health economy planner and for facility administrators. The data required includes an estimation of daily number of cases, hospitalisations, admissions to ICU, mortality, costs, QALYs and cost-effectiveness, by use of economic methodology, which may be valuable when the information network fails, is delayed or is inexistent.

The papers cover the main areas where information is needed in a time-frame progress:

1/ How will the outbreak behave? How many casualties are expected? What resources will be required? This implies the need to be ready to plan arrangements with private hospitals for healthcare provision, the analysis of funeral and cremation capacities and what to do in case

of this being surpassed, the amount of, and time frame for, personal protection equipment acquisition, the reinforcement of personnel, etc.

2/ Vaccination and fake news. How the extensive expansion of fake news could alter the preventive plans after vaccine availability. How many people will get vaccinated? How much will the budget be for vaccination? How to reduce fake news, particularly when publicised by health care professionals subject to the ethical code. Should all this be regulated? Could vaccination be made mandatory? Will it be cost-effective? Will it be possible to set additional priorities, e.g., to include children and pregnant women in early vaccination plans?

3/ How much will COVID-19 cost the health care system?

4/ How well are the personnel accepting and bearing the extra workload that the pandemic is causing them? What are the main concerns of frontline staff, i.e., nurses, after the coronavirus outbreak? Is there a way to assess their worries objectively? Is it possible to obtain statistically significant results on that issue, using bibliometric methods?

The structure of the text follows the regulations of the Universitat Politècnica de València (UPV) for a doctoral thesis by publications, with an introductory chapter, a second chapter with the description of the articles —including the formatting requirements of the publishers and their own reference styles. There is no copyright issue, as all the publications included in the thesis are open access. Additional unpublished but complementary work is also included, followed by a discussion chapter and the concluding chapter. After the references there are additional comments on copyright, formatting, and stylistic details.

The length of this text, following the UPV regulations for this type of doctoral thesis (for published works) has been kept at around 20,000 words, but the articles have been excluded from the word count.

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Chapter 2
Publications

2.1. PAPER I. (2020). COVID-19 Healthcare Planning: Predicting Mortality and The Role of the Herd Immunity Barrier in the General Population

2.1.1. Introduction to paper I.

From the beginning of the expansion of the SARS-CoV-2 virus, some differences to the previous MERS-CoV-1 became evident. Unlike the latter, which emerged in the Middle East (Saudi Arabia and Jordan), where several patients had had close contact with camels (although human-to-human transmission was proven early) and had some geographical limitation (but extending outside the Middle East to the Republic of Korea and other areas), the COVID-19 disease spread worldwide very rapidly and regardless of the chain of transmission of the first cases, the contagion has been primarily human-to-human and its spread pandemic in nature (Azhar et al., 2014; Memish et al., 2020).

This rapidly expanding pandemic caused overload of the healthcare systems, and serious difficulties in the collection, storage, and release of information. Nevertheless, health economy and the management of healthcare facilities require information for decision making and action planning. Thus, as an example, if the forecast of deaths exceeds the capacity of funeral services and of crematoria or cemeteries, special measures need to be taken, probably with the help of the army and a special action plan for the bodies.

The second question that needed to be answered from the outset was whether to rely on herd immunity or not, as some countries such as the United Kingdom initially seemed to have chosen to do. The consequences of such a decision for the economy in general, and for health economy in particular, would be of fundamental importance.

Therefore, for the initial phase planning it was necessary to answer questions such as:

1/ How long will the disease last?

2/ Will there be one outbreak or more?

3/ How many cases will need to be treated and by what means?

4/ What will the mortality be?

5/ Is it possible to use herd immunity as a barrier?

The answer to these questions needed appropriate information or else the best estimation. However, the ability to collect and provide accurate information was overwhelmed by the speed and severity of the pandemic, as already commented. Some decisions, such as to consider deaths caused by COVID-19 only after confirmation by Polymerase Chain Reaction (PCR) testing, reduced the number of official casualties, something acknowledged by the National Institute of Statistics (INE), which on 10 December 2020, added 13,036 cases as

suspected of having died from COVID-19, bringing the total number of deaths to 45,684 which is 18,557 more than the figure provided by the health authorities in that period (Instituo Nacional de Estadística (INE) [National Institute of Statistics of Spain], 2020)

The incongruence of the reported data is evidenced in the following figures:

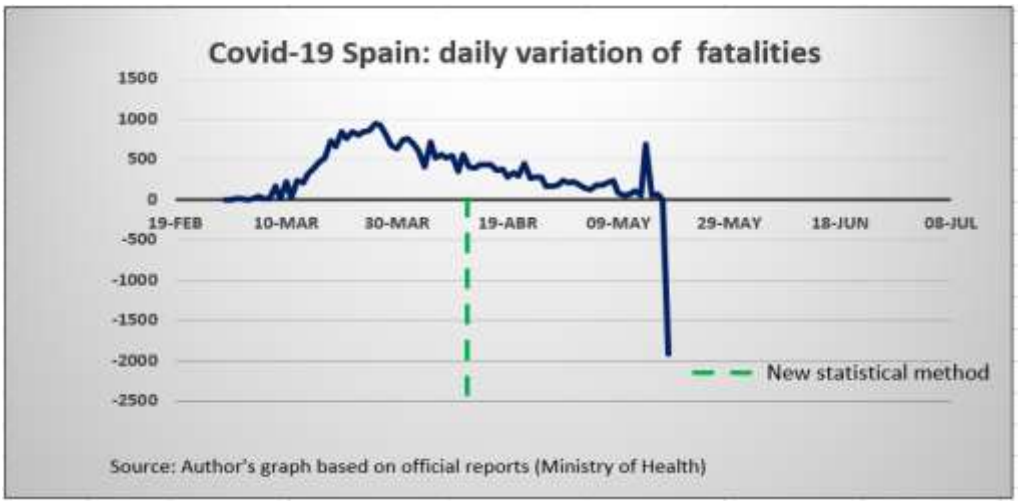

Figure 2.1.1. Inconsistency of health authorities' reported casualties. Source: Authors' graph based on official reports.

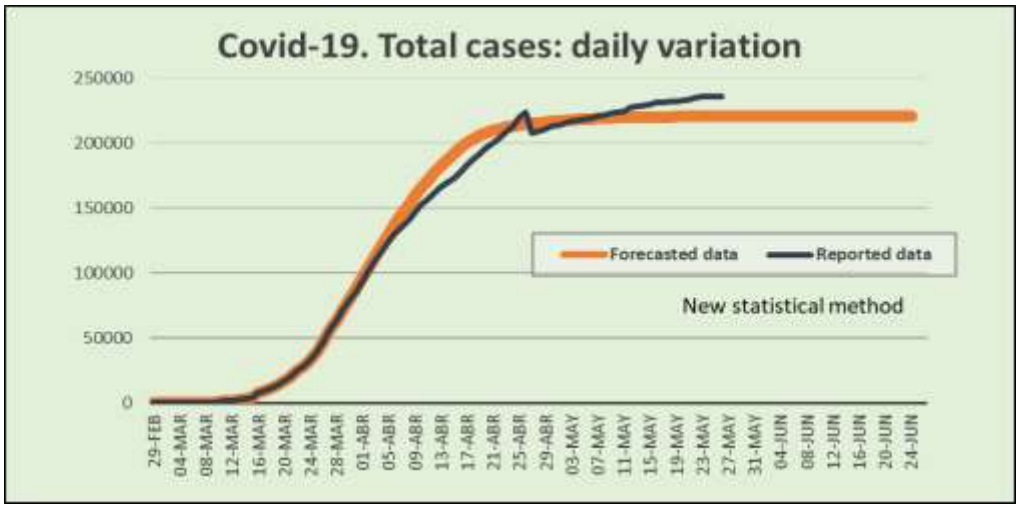

Figure 2.1.2. Inconsistency of health authorities' reported total number of cases. Source: Authors' graph based on official reports.

During the recording of information, new statistics were implemented, first at governmental level and then the responsibility was transferred to the regions (Comunidades Autónomas) with the consequent interruption of continuity.

This paper was born from the idea of providing an approach to the real figures showing evolution, mortality, and of forecasting the role of herd immunity as a barrier for the COVID-19 in Spain. This later point was not so crucial for Spain as there was an ongoing serological survey, but it will serve as a test to analyse the precision of the estimation.

Despite the above-mentioned inconsistencies, the official figures tend to show a pattern that could be useful for the model.

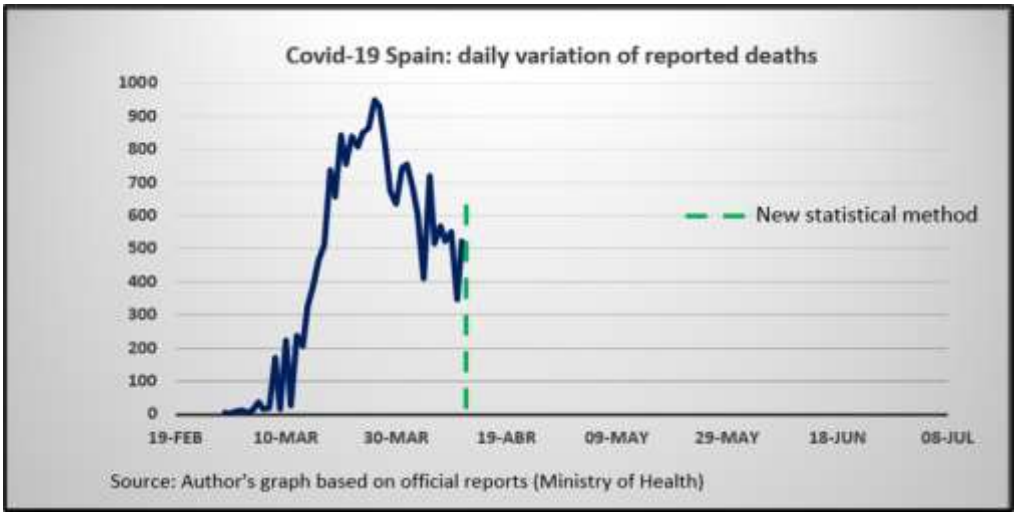

Figure 2.1.3. Daily variation of reported deaths. Source: Authors' graph based on official reports.

Therefore, for the model we count on this information, on the evolution from other RNA virus patterns, admissions data, and data obtained using the Best Adjustment of Related Values (BARV) method, which attempts to adjust reliable figures within a range and calculate other less reliable related values by means of an iterative adjustment, so that the possible errors of all the variables are minimised, thus minimising all deviations. This was done using data from previous publications with information on the infection fatality rate (IFR), case fatality rate (CFR), percentage of admissions, deaths, etc. (Italian Task Force COVID-19, 2020; Wu & McGoogan, 2020). Some reports in which the entire population was monitored, such as in the Prince of Diamond Cruise, were particularly enriching (Rajgor et al., 2020).

More weight was given to two sources that were deemed more reliable. The first one was the Mortality Monitoring (MoMo) database (MoMo-Rp 17/5-Ministerio de Justicia [Spanish Ministry of Justice], 2020), as in countries such as Spain, and other developed countries, it is virtually impossible to die without being recorded.

For the second, considering that there is a national health system, with a large majority of the population being treated in public hospitals, and that hospitalisations are recorded in the hospital information system (HIS), the information from the hospitals was considered reliable. This value may be somewhat underestimated as some patients have been admitted to private hospitals, which may or may not be included in the statistics, but in any case, their impact on the final forecast was not considered to be relevant.

So, the questions that this paper intended to answer were:
1/ Is it possible to overcome the limitations of the collapse of information in the networks of health information and estimate with some reliability the situation in terms of number of patients affected and mortality?
2/ Is it possible to estimate if herd immunity could play a role as barrier for the infection? As mentioned, this question was already being analysed by the Institute Carlos III, with two serological surveys (Instituto de Investigación Carlos III-[Research Institute Carlos III] (a), 2020; Instituto de Investigación Carlos III-[Research Institute Carlos III] (b), 2020), but our idea here was to see how accurate our early forecast of this issue would be, as it may not always be possible to test thousands of population for serological studies.

2.1.2. Paper text. Author's version format.

COVID-19 Healthcare Planning: Predicting Mortality and the Role of the Herd Immunity Barrier in the General Population.

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Abstract: Using a mathematical model for COVID-19 incorporating data on excess of mortality compared to the corresponding period of the previous year obtained from the daily monitoring of mortality in Spain (MoMo), the prediction of total number of casualties in Spain for the first outbreak has been computed. From this figure, and following a stepwise meta-analysis of available reports, the case fatality rate (CFR) and the infectious case fatality rate (IFR) for the outbreak have been estimated. As the impact of age on these rates is notable, it is proposed to include an age-related adjusted fatality ratio in future comparative analyses between studies, calculated by adjusting the results by risk ratio to a reference age band (e.g., 60–69). From the casualty figures, and the corresponding CFR and IFR ratios, the forecast of serologically positive cases in the general Spanish population has been estimated at approximately 1% (0.87–1.3%) of the samples. If the data are confirmed by the ongoing study of the Carlos III Institute, until a vaccine is found, the immunity acquired in the general population after the infectious outbreak is far from the 65–70% herd immunity required as a barrier for COVID-19.

Keywords: healthcare planning; health economy; herd immunity; mathematical epidemiology; COVID-19; case fatality rate; infectious fatality rate; relative risk ratio; predictive modelling.

1. Introduction

In December 2019, China reported 27 cases of pneumonia of unknown origin. The agent causing this pneumonia was identified as a new virus named SARS-CoV-2. The disease associated with this virus has been called COVID-19. On March 11, the World Health Organization (WHO) declared the pandemic as global. Since the beginning of the epidemic to the date of this paper (April 20), more than two and a half million cases have been reported worldwide, and more than 200,000 in Spain.

Unlike other pandemics that originated in less economically developed nations, COVID-19 has emerged in several of the world^{0}s largest economies, spreading across the globe causing enormous disruption to economic, working, and social life. To analyze the impact on healthcare economics and policies, accurate and reliable data are essential.

As has been recognized by the health authorities themselves, the official data on COVID-19 are incomplete and inconsistent. Reported values are far from what may be obtained with mathematical modeling [1,2]. For that reason, we have elaborated our data based on more reconcilable information, the mortality. According to the daily monitoring of mortality in Spain report from the Ministry of Justice (MoMo), there has been an unexpected increment of mortality figures when compared with the same period in 2019 [3]. Given that there are currently no other epidemic

diseases, we assume that this increment corresponds to undetected cases of COVID-19, directly or indirectly. Based on this hypothesis, we estimated the expected casualties, CFR (case fatality rate), IFR (infectious case fatality rate), and the percentage of population which may result in positive serological testing for COVID-19 in Spain, using a mathematical model, and a meta-analysis with easy obtainable data from previous reports. This mathematical model is applied to the infectious outbreak occurring in Spain starting on March 9. This proceeding may be especially useful for making estimates in the event of a disease outbreak in the coming months. This estimation is used as a guide to consider the convenience of health policies based on herd immunity in Spain.

2. Material and methods

Two different mathematical procedures are used. The first one starts on the date with more than 30 new casualties per day and extends to the calculated point with less than 30 new deaths per day, assuming neither significant changes in the evolution process nor rebounds and a lock-down of 45 days. The number of deaths at a given time *t* (today) is the sum of the past infections weighted by their probability of death, where the probability of death depends on the number of days since infection.

Using a previous reported methodology [4], the expected number of deaths, *dt*, on a given day *t*, is given by the following discrete sum:

$$dt = \sum_{\tau=0}^{t-1} c_\tau \pi_{t-\tau} \quad (1)$$

where c_τ is the number of new infections on day τ and where $\pi_{t-\tau}$ is the probability of death for day *t* for those getting infected on day τ*;* it may be discretized via

$$\pi_s = \int_{s-0.5}^{s+0.5} \pi_m(\tau) d_\tau \quad (2)$$

for $s = t-\tau$ for $s = 2, 3, \ldots$ ending when the daily casualties are <30, and

$$\pi_1 = \int_{0.5}^{1.5} \pi_m(\tau) d_\tau \quad (3)$$

In forecasting new outbreak data at a time t, i(t), it could be interesting to consider the use of time-related exponential growth rate (r) models [5].

$$i(t) = i_0\, e^{rt} \quad (4)$$

where i_0 is the expected number of infected cases at time $t = 0$.

The cumulative incidence *I(t)* is the integral of *i(t)* over the period 0 – *t*

$$I(t) = \int_0^t i(s)ds = \int_0^t i_0\, e^{r(t-\tau)}\, d(t-\tau) = i_0\,(e^{rt} - 1)/r \quad (5)$$

The cumulative incidence may be adjusted to the date of report by a factor *u* dependent on the parameters of the delay distribution. For estimating the distribution of time delay from onset of disease to death, the authors have used correct truncation and modelling of a log-normal distribution [6].

In case of a log-normal distribution $f(t; \theta)$, with parameters $\theta_d\{a_d; b_d\}$, the factor $u(r; \theta_d)$ is the multiplying parameter for adjustment of *I(t)* by date of report *t*, to the time from onset to death. The factor *u* results from [5]:

$$u(r;\theta d) = \int_0^{\infty} exp(-rs) f(s;\theta_d) ds \quad (6)$$

It is also possible to evaluate the effects of lockdown with transmission models using a Bayesian framework and jointly infer parameters, as have done the French Pasteur group [7] (p.12), in our case for 45 days of lockdown. Other models may analyse the serial interval (the time between symptom onset of a primary and secondary cases). However, due to the uncertainties about real infected cases, this mathematical approach has been used only as a test to confirm if the approximate data obtained with the meta-analysis were consistent.

3. Results

According to information from MoMo [3], unexpected versus real death values reported for the period from March 17 to April 18 were respectively 25,907 and 63,676 (all-death causes), representing 40.7% of the total (Table 1). The expected value of 37,769 is consistent with the National Institute of Statistics of Spain (INE) 2018 [8] report of a daily average of 1172 deaths. COVID-19 deaths reported by the Ministry of Health (corresponding to April 18) were 20,043 cases (Ministry of Health, Spain, daily release information: https://www.mscbs.gob.es/profesionales/saludPublica/ccayes/alertasActual/nCov-China/home.htm (accessed April 19, 2020).

Table 1. Spain: Under-estimation of causalities (March 17 to April 18) in official report.

Total Cases	Expected Cases	Unexpected	Reported COVID-19	Report Under-Estimation	
63,676	37,769	25,907	20,043	5864	29%

Source: Authors' computation with information from MoMo, Ministry of Justice [3,8].

With the adjusted values of casualties of 45 days, starting on March 9, a prediction curve for the estimated period of pandemic has been elaborated (Figure 1).

Figure 1. COVID-19: evolution of adjusted (standardized) casualties per million population (PMP). Authors' forecast based on first 45 days of outbreak starting March 9.

The evolution follows a right skewed curve (skewness = 0.53, Kurtosis = −1.10) with mean = 9.4058 and standard error of the mean (SEM) = 1.003517915. This study is point-estimate focused on cumulative data (casualties) at the end of the outbreak (defined in this study as less than 30 new daily deaths in Spain).

If the total predicted period of this (first) outbreak of 69 days is correct (Figure 1), the adjusted overall total mortality in Spain would be about 30,568 cases (27,307–33,830). This would

correspond to overall casualties for this outbreak of 649 per million population (PMP) (0.0649%). [9]

The estimation for regions (CCAA), based on the relative ratio of reported casualties PMP, is presented in Table 2, including total number of casualties and case fatality rate adjusted PMP. This computation assumes a CFR equally distributed among the regions, and only dependent on population, something unproved at present time.

Table 2. Spain: estimation of regional overall outbreak casualties per million population (PMP) over a period of 69 days.

Regions (CCAA)	Total Casualties	CFR PMP	Regions (CCAA)	Total Casualties	CFR PMP
Andalucía	1501	178.7	Valencia	1563	312.7
Aragón	939	708.6	Extremadura	556	523.4
Asturias	328	321.8	Galicia	519	192.4
Baleares	231	192.5	Madrid	10,442	1562.0
Canarias	173	77.8	Melilla	3	31.3
Cantabria	241	414.5	Murcia	167	112.0
Castilla La Mancha	3071	1506.7	Navarra	568	870.7
Castilla y León	2196	913.9	País Vasco	1621	743.1
Cataluña	6019	790.0	La Rioja	415	1.320.3
Ceuta	5	62.4			
			Spain (Overall)	30,568	649.0

Source: Authors' computation with information from INE [8] and MoMo, Ministry of Justice [3].

For the meta-analysis procedure to estimate seroprevalence, it is necessary to determine the proportion of symptomatic versus asymptomatic patients. The two key figures, CFR and IFR, are forecasted based on previously available reports.

The report from the Diamond Princess cruise ship, where an outbreak occurred, and which was quarantined from January 20 to February 29, 2020 [10] is a very revealing paper. From a total of 3711 people on board (passengers and crew), 705 became sick (19.0%), and seven died (a casualty in the sample of 0.003%). On February 20, 2020, 3063 PCR tests were performed with a positive result of a total of 634 people (20.7%), with 476 of them over 60 years. Of the 634 confirmed cases, approximately half of them where asymptomatic (306). Of these 634 cases, 313 cases were female. The age pattern was: 6 aged 0–19 years (0.94%), 152 aged 20–59 years (23.98%) and 476 aged 60 years and older (75.08%), with a genetic diversity from 28 countries [11]. The data were statistically modelled, and observations treated as survival data with right censoring. The probability of being asymptomatic once infected and the infection time for each case were estimated using a Hamiltonian Monte Carlo algorithm. The estimated total number of true asymptomatic cases was 113.3 (95% credible interval: 98.2–128.3%) and the estimated asymptomatic proportion among all infected cases 17.9% (95% credible interval: 15.5–20.2%). The results are summarized in Table 3.

Table 3. Epidemiological data from Diamond Princess cruise.

Sample Size		PCR Positive	Over Infected			Over PCR +	Over Sample
			True Asymp	Symp.	IFR	CFR	Casualties
		21%	18%	82%	1.11%	1.35%	0.23%
(n)	3063	630	113.3	516.7		7	

Source: Authors' computation with data from [10,11]. IFR: infectious fatality rate. CFR: case fatality rate.

This reported probability of death following the development of symptoms (1.35%) is very close to that published in China, analyzing 79,394 cases, with 1.4% (0.9–2.1%) [12] and to the results (1.6%) in another report [13]. Starting from the death figure, this allows us to estimate the number of symptomatic cases. However, as seen, the crude mortality percentage is about 4 times higher than that previously found for the general population of 0.06%. This underlines the

importance of age band. As mentioned, more than 75% of the PCR-detected cases were aged 60 or older. All 7 deaths reported from the Diamond Princess cruise were patients of 70 years or more [14].

In the second study used in the meta-analysis, one from China with 72,314 case records [15], CFR increased to 8% in patients aged 70–79 years, and 14.8% in patients aged 80 or more years, with an overall CFR of 2.3%. Other papers report CFR values around 5% [7,16,17]. Once more, the age pyramid is of paramount importance in mortality (Table 4), as is access to ICU, particularly in aged people.

Table 4. Epidemiological data from Chinese Centre for Disease Control and Prevention.

Age	Casualties	Cases	% CFR (95% CI)
≤9 years	0	416	0
10 to 19 years	1	549	0.18 [0.03–1.02]
20 to 49 years	63	19,790	0.32 [0.25–0.41]
50 to 59 years	130	10,008	1.3 [1.1–1.5]
60 to 69 years	309	8583	3.6 [3.2–4.0]
70 to 79 years	312	3918	8.0 [7.2–8.9]
≥80 years	208	1408	14.8 [13.0–16.7]
Overall	1023	44,415	2.30

Source: Authors' computation with data from Wu & McGoogan [15].

In the stepwise process, it must be considered that age, gender, and comorbidity, particularly cardiovascular, play important roles in the final CFR result. Oke and co-workers reported data from the Italian Health Ministry scientific adviser (Professor Walter Ricciardi) indicating that 88% of Italian death certificates related to COVID-19 included at least one pre-morbidity and frequently two or three [18]. Consequently, the evaluation of age, gender, and comorbidity profile becomes crucial when comparing different data series. The Italian series dated March 26, including 73,780 cases [19], provide CFR information closer to our Mediterranean society (Table 5):

Table 5. Epidemiological data from Italy on 26 March 2020.

Total Cases					
Age Band	**# Cases**	**% Age Band**	**# Death**	**% Death/ Age Band**	**% CFR**
0–9	424	0.6	-	0.0	0.00
10–19	510	0.7	-	0.0	0.00
20–29	2713	3.7	-	0.0	0.00
30–30	4959	6.8	17	0.2	0.34
40–49	9167	12.6	67	1.0	0.73
50–59	14,335	19.7	243	3.6	1.70
60–69	13,149	18.1	761	11.2	5.79
70–79	14,090	19.4	2403	35.3	17.05
80–89	10,929	15.0	2702	39.7	24.72
≥90	2517	3.5	608	8.9	24.16
Total	72,793	100.0	6801	100.0	9.34
Males					
Age Band	**# Cases**	**% Gender**	**# Death**	**% Death/ Gender**	**% CFR**
0–9	244	57.5	-	0.0	0.00
10–19	261	51.2	-	0.0	0.00
20–29	1203	44.3	-	0.0	0.00
30–30	2465	49.7	14	82.4	0.57
40–49	4597	50.1	49	73.1	1.07
50–59	7998	55.8	190	78.2	2.38
60–69	8755	66.6	606	79.6	6.92
70–79	9309	66.1	1846	76.8	1.83
80–89	6195	56.7	1808	66.9	29.18
≥90	877	34.8	273	44.9	31.13
Total	41,904	57.6	4786	70.4	11.42

Table 5. *Cont.*

Total Cases					
Age Band	**# Cases**	**% Age Band**	**# Death**	**% Death/ Age Band**	**% CFR**
Females					
Age Band	**# Cases**	**% Gender**	**# Death**	**% Death/ Gender**	**% CFR**
0–9	180	42.5	-	0.0	0.00
10–19	249	48.8	-	0.0	0.00
20–29	1510	55.7	-	0.0	0.00
30–30	2494	50.3	3	17.6	0.12
40-49	4570	49.9	18	26.9	0.39
50–59	6337	44.2	52	21.4	0.82
60-69	4394	33.4	154	20.2	3.50
70–79	4781	33.9	555	23.1	11.61
80-89	4734	43.3	894	33.1	18.88
≥90	1640	65.2	334	54.9	20.37
Total	30889	42.4	2010	29.6	6.51

Source: Authors' recalculation of data from records with complete information (987 cases excluded) published by the Higher Institute of Health (Istituto Superiore di Sanità, ISS). CFR case fatality ratio [19].

As to better include age band in future estimations, the report from The Centre for Evidence-Based Medicine [18] reproduces the whole series of the Italian report [19] describing the statistics as «a grouped-binomial logistic regression with log-link function with main effects for age-band and sex (no two-way interaction terms). Deviance statistic is 30.9 on 6 degrees of freedom» (para.16) providing a table of risk ratio (Table 6) taking age band 60–69 as a reference.

Table 6. COVID-19 risk ratio for gender and age band.

Category	Risk Ratio	95% CI
Age 30–39	0.06	[0.038–0.10]
Age 40–49	0.14	[0.11–0.17]
Age 50–59	0.31	[0.27–0.35]
Age 60–69 (reference)	1	-
Age 70–79	2.95	[2.7–3.2]
Age 80–89	4.47	[4.1–4.8]
Age 90+	4.83	[4.4–5.3]
Female	1	-
Male	1.66	[1.58–1.74]

Source: Centre for Evidence-Based Medicine research with data from Italian Task Force COVID-19 [19].

4. Discussion

During the COVID-19 outbreak, data reported by the authorities has proved to be inconsistent. We have estimated an under-reporting of the number of deaths of 29%, close to what has been found in the UK with inconsistencies of about 24% [20], and in other countries [21,22]. A median time delay of 13 days from illness onset to death (17 days with right truncation) [6], and the median basic reproduction number (*R*o) 4–6, not far from (2–5), found in other SARS viruses such as the Singapore outbreak [5,23,24], have been reported. The casualties we found for the period studied (649 PMP) are also consistent with other reports [9], and the characteristics of the curve, including a period of about 10 weeks, is consistent with an RNA virus pattern [25].

In cases of incomplete information, such as in the COVID-19 outbreak, death rate may provide the more reliable information to begin with, but one of the important points when comparing

different fatality ratios is to analyse data adjusted to the corresponding age band. In this regard, we propose to include an additional reference index, the age-adjusted case fatality ratio (aaCFR), based on risk ratio, setting an age band (e.g., 60–69) as reference. Taking the age bands into consideration, the estimation of the evolution of casualties may be more precise. Once the number of casualties has been determined with the mathematical model, the meta-analysis using available data from the literature allows the estimation of CFR, IFR, and seroprevalence.

Based on the above-mentioned reports, the CFR in Spain could be 4–7%, which is half to one third of the 15% CFR reported by WHO for SARS [26] (p.10), but according to the report, «global case-fatality ratio of 11% was recorded at the end of the outbreak». Consequently, it may be that both SARS outbreaks are not that different in fatality rate.

In the study of the Diamond Princess cruise ship, the IFR result of about half the CFR [10,11], (CFR 2.3% (CI 95% 0.75–5.3%), and IFR 1.2% (CI 95% 0.38–2.7%)), data from Wuhan, and other reports, including WHO [27,28], allow us to forecast that IFR is about half of CFR. This ratio is supported by a computation of data, using Bayesian Markov-chain Monte Carlo methodology, in an age-stratified CFR and IFR model, which resulted in an (adjusted) IFR/CFR ratio close to 0.5 (0.478) [29]. The IFR could be analysed by predicting attack-rate for age groups [4], but as the main interest here was to move from mortality data to overall population affected in order to evaluate the gross number of possible infected patients, this age-band analysis is not essential. It is difficult to make a comparison with influenza A (H1N1), as a review of 77 CFR estimations from 50 studies showed a substantial heterogeneity in ranking, from less than 1 to more than 10,000 deaths per 100,000 cases or infections [30]. The official report of the Spanish Surveillance flu group computed a CFR of 0.43 deaths per 1000 cases for the 2009 (H1N1) pandemic [31].

The number of infected patients, assuming most of them will develop herd immunity (natural immunity)—something far from being proved—could be a gross indirect index of the extension and severity of future outbreaks.

Approximating mostly to the Italian report, a crude CFR of 10% over the 30,568 casualties estimated by mathematical modelling at the end of the outbreak will represent a crude IFR value of 5% at most, or around 0.6 million infected patients including both symptomatic and asymptomatic cases (1.3% of a Spanish population of 47.1 million), a figure about half the lowest range of the prediction by the Imperial College Report [4] for Spain. If the WHO lower estimation of CFR/IFR is considered (1/3), then the value is 0.4 million infected patients (0.87% tests will result positive).

Another indirect and approximate estimate of the highest percentage of seropositive cases can be obtained based on the number of hospitalized patients in Spain, whose percentage in relation to the total number of declared cases is 55% [32]. Let us assume that this percentage is not the result of a health policy and protocols in Spain (or Italy) different from those of China and other countries, but rather the result of incomplete information on cases. Let us assume that the number of hospitalized patients corresponds in reality to only 15–20% of the infected population, in line with the WHO report [28]. Over an estimation of about 225,000 cases estimated at the end of this outbreak (in the terms of less than 30 new deaths per day as mentioned), this will represent approximately 123,000 hospitalized patients; if this value is only 15–20% of total symptomatic cases, it will mean 819–615 thousand cases. Taking the highest value and the highest ratio of symptomatic versus asymptomatic cases (0.5), that extreme limit would give an estimation of about 1.2 million patients who have come into contact with the virus (either with or without symptoms), and assuming all their tests will be positive, this upper value estimation represents only 2.6% of the population.

Consequently, serologic analysis is expected to show immunity about 0.87–1.3% of the population, a value close to other preliminary studies, such as the one from Stanford University in Santa Clara with 3324 cases and a result of 1.5% (exact binomial 95% CI 1.1–2.0%). Their test

performance specificity was 99.5% (95% CI 99.2–99.7%) and sensitivity s 82.8% (95% CI 76.0–88.4%). The unweighted prevalence adjusted for test performance characteristics was 1.2% (95% CI 0.7–1.8%). After weighting for the population demographics of Santa Clara County, the prevalence was 2.8% (95% CI 1.3–4.7%), using bootstrap to estimate confidence bounds [33]. In our case, less than 3%.

A value about 2–3% positive results in testing the general population has been suggested as a realistic result by the General Director of WHO, Dr Tedros Adhanom Ghebreyesus [27], and this seems to be congruent with the first results obtained in the Netherlands study. Higher percentages (14%), such as reported in the German study with a limited sample of 500 subjects in Heinsberg [9], have been criticized as possible false caveats. The low rate of casualties (0.37%) reported in that study is also to be noted, far from the overall reported fatality rate in Germany of 2% [34]. There is also a surprising ratio of infected people (2%) versus those with antibodies (14%), discrepant with other reports (as commented above) suggesting asymptomatic patients to be about 1/3 or 1/2 of the number of cases with clinical symptomatology.

5. Conclusions

The COVID-19 pandemic outpaced capabilities to control and record cases and deaths and reporting of data has been inconsistent in many official records [1,2,35]. Clinical assumptions have been made without serological confirmation and many casualties in nursing or home care institutions have not been recorded as related to COVID-19. For these reasons, our study is based on mortality data compared to the period of the previous year [3] and combined with an epidemiological mathematical model which allows estimating the number of cases and deaths at the end of this (first) outbreak. Then, using this result and the relative ratios from other studies, a meta-analysis has been developed to estimate seroprevalence. The heterogeneity of the data in different reports may be, in part, related to the different incidence of the disease according to age bands [13], and an adjustment for relative risk for future reports is proposed in the future. As an important point in health planning is to estimate whether herd immunity may represent a barrier to COVID-19 in Spain, our results based on a meta-analysis contrasted with a mathematical model prediction of approximately 1% of positive tests in the general population (data that in the future may be contrasted with the results of the ongoing study carried out by the Instituto Carlos III). Even considering an extreme value of 2.6%, obtainable by another indirect method, our weighted range (1% to 3%), in line with that reported by the WHO, is very far from the 65–70% necessary for herd immunity to be an effective barrier for COVID-19. As stated by Australian epidemiologist Gideon Meyerowitz–Katz, without vaccination, there is no place for herd immunity as a barrier for COVID-19 [36].

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Conflicts of Interest: The authors declare no conflict of interest. The authors declare that they have no affiliations with or involvement in any organization or entity with any financial interest in the subject matter or materials discussed in this manuscript.

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2.1.3. Comments to paper I.

The basis of this paper was to provide estimations of the indexes based on certain available recorded information considered to be more reliable, while incorporating other less well-founded information, through a process of adjusting the values, as commented, until minimisation of deviations. We suggested early on that the differences found among reports could be related to differences in age patterns, proposing an adjustment ratio taking 60–69 as reference (age-adjusted case fatality ratio [aaCFR]),

The results became an early report on seroprevalence with an estimation of about 1 to 3% of the population to be serologically positive and thus protected against COVID-19, a value far from the 65–70% required for herd immunity to be used as barrier. The real data obtained after population serological test studies in Spain indicated about 5%:

> The estimated prevalence of IgG antibodies against SARS-CoV-2 at Spain is 5.0%. (IC 95%: 4.7–5.4). The prevalence is similar in men **5.0%** (IC 95%: 4.7–5.4%) and women: 5.1%; (ICI [sic] 95% IC: 4.7–5.5%). By age, the prevalence is lower in infants children and youth, while there are moderate differences among higher age groups. (Spanish Government, 2020)

Also notable in this paper is that it provided a better approach to mortality, as later recognised by the INE, which many months later incorporated data close to these early estimations.

Consequently, in terms of providing initial estimations, the results were reliable enough for the purposes planned.

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2.2. PAPER II. (2021). COVID-19, Fake News, and Vaccines: Should Regulation be Implemented?

2.2.1. Introduction to paper II.

Locked down within the confines of the walls of their homes and with powerful communications systems on hand, it is not surprising that citizens have spent an enormous number of hours searching for information about what was going on, which has led to understandable

confusion. The level of fake news and misinformation regarding COVID-19 increased to the point of creating concern in the World Health Organization, the European Union, and other organizations that have considered ways and channels to reduce scientifically unfounded information and the consequent risk of harmful acts (e.g. ingestion of bleach) or omissions (refusal to be vaccinated) resulting from misinformation with potential health hazards (European Commission, 2020; World Health Organization (WHO), 2020b).

This is not to say that false information was not present before the pandemic, as shown by the Flash Eurobarometer 464 (European Commission, 2018):

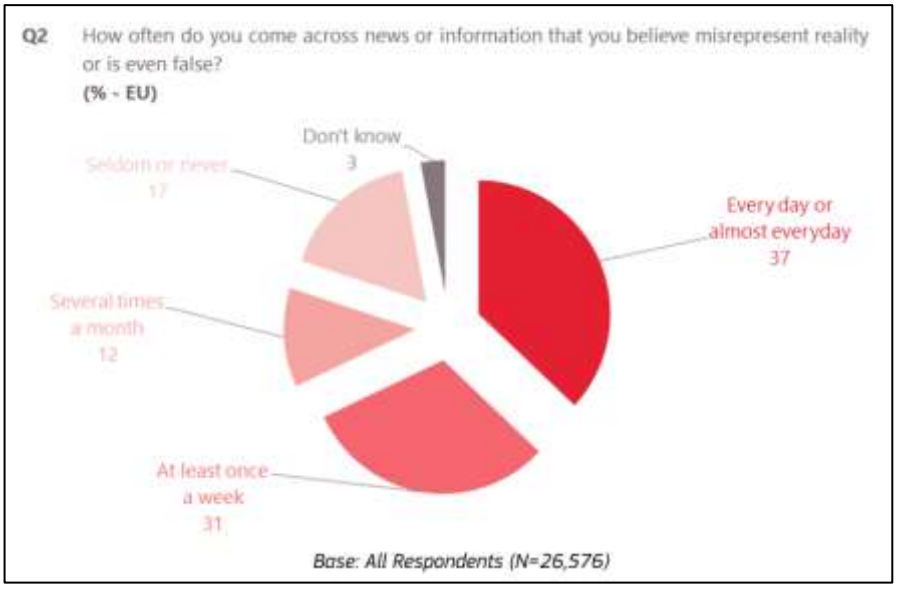

Figure 2.2.1. Frequency of fake news in Europe 2018. Source: Flash Eurobarometer 464.

Regarding Spain:

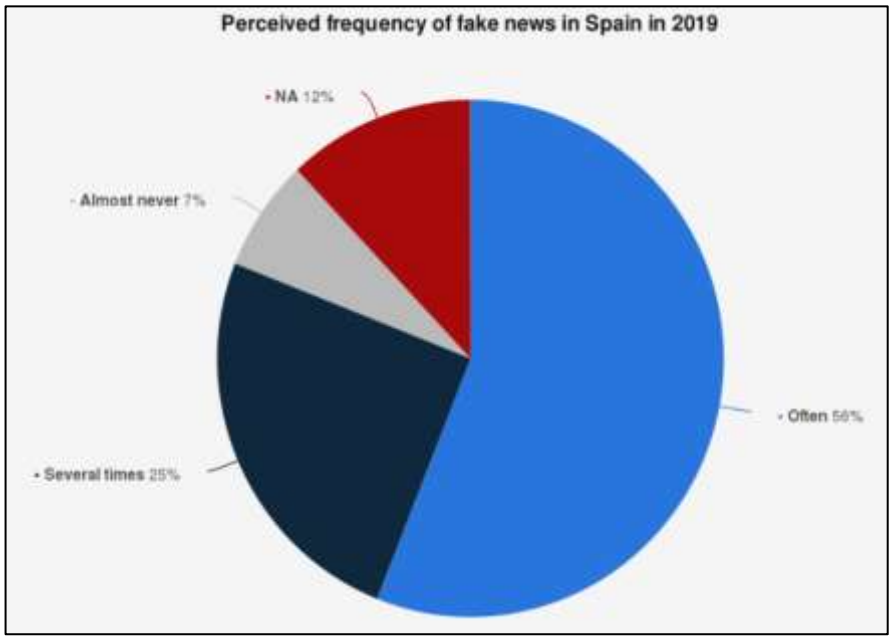

Figure 2.2.2. Perceived frequency of fake news prior to COVID-19 in Spain. Source: Fundación BBVA © Statista, 2019.

According to surveys most respondents feel confident in their capacity to recognise fake news.

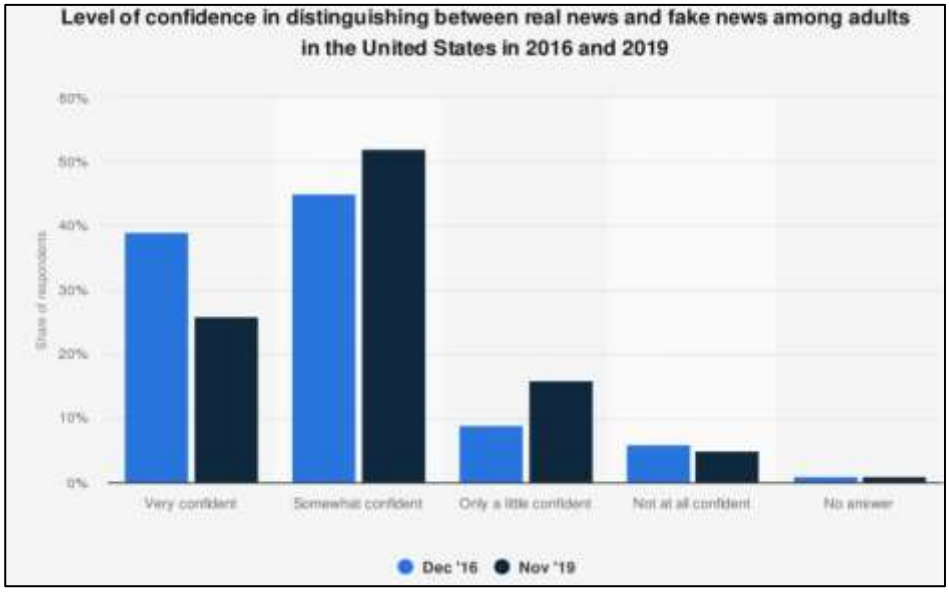

Figure 2.2.3. Confidence in distinguishing real and fake news in the USA. Source: Pew Research Centre ® Statista, 2019.

The situation after the pandemic changed, with a notorious increase of fake news circulation, both in the USA and in Europe:

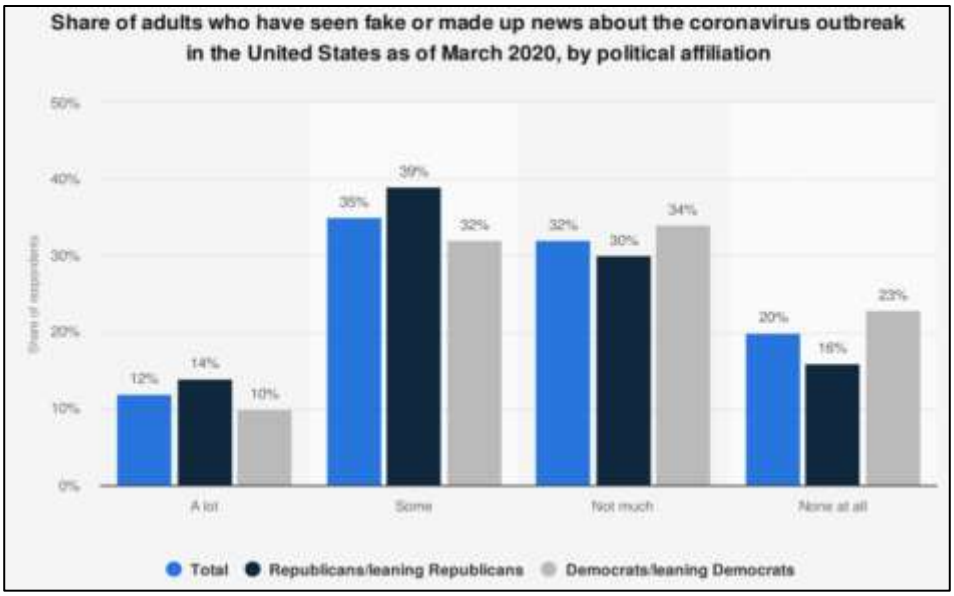

Figure 2.2.4. Fake news on coronavirus in the USA (March 2020). Source: Pew Research Center ® Statista, 2019.

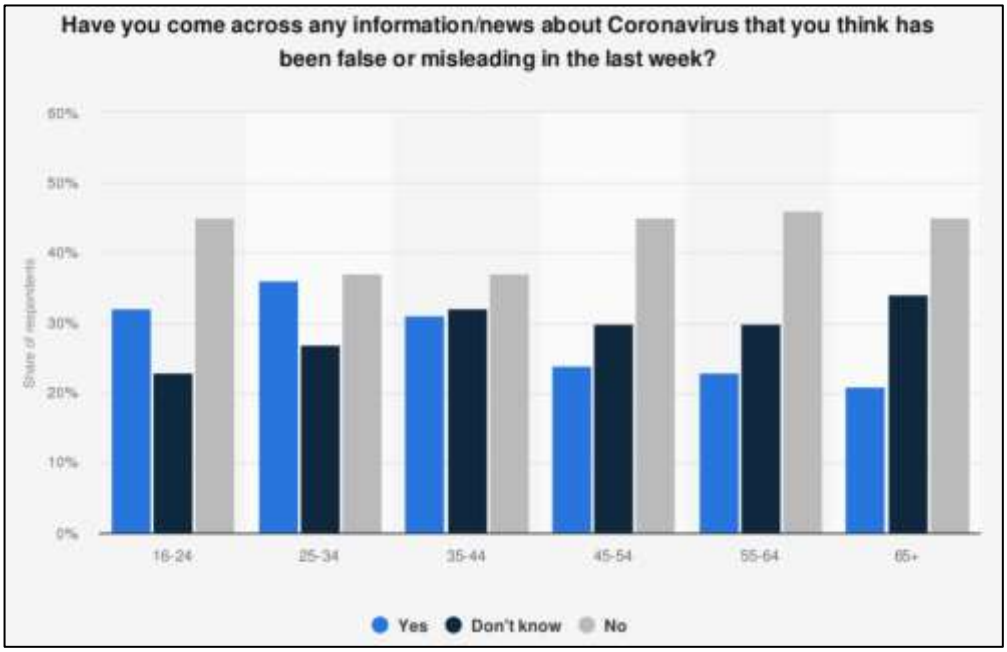

Figure 2.2.5. Fake news on coronavirus in the UK as of September 2020. Source: Ofcom Populus ® Statista, 2020.

For the perceived reliability of the news, the source is important. News released by doctors, scientists and health experts is considered as the most reliable:

Table 2.2.1

COVID-19: reliability of news and information by source Spain 2020

Scientists, doctors, other health experts	7.8
World health organizations	7.3
National or regional health organizations	6.7
Media	5.6
Search engines	5.3
National government	5.0
Friends	4.8
Video platforms	4.4
Political representatives	4.2
Social networks	4.1
Messaging apps	4.0
Citizens (non-friends)	3.5

Note. Source: Digital News Report España, 2020. Universidad de Navarra (Centre for Internet Studies and Digital Life School of Communication) rating scale ranges from 0 (= not at all reliable) to 10 (= totally reliable). June 2020 © Statista 2020.

A relevant percentage of the respondents consider that fake news should be considered as a criminal offence:

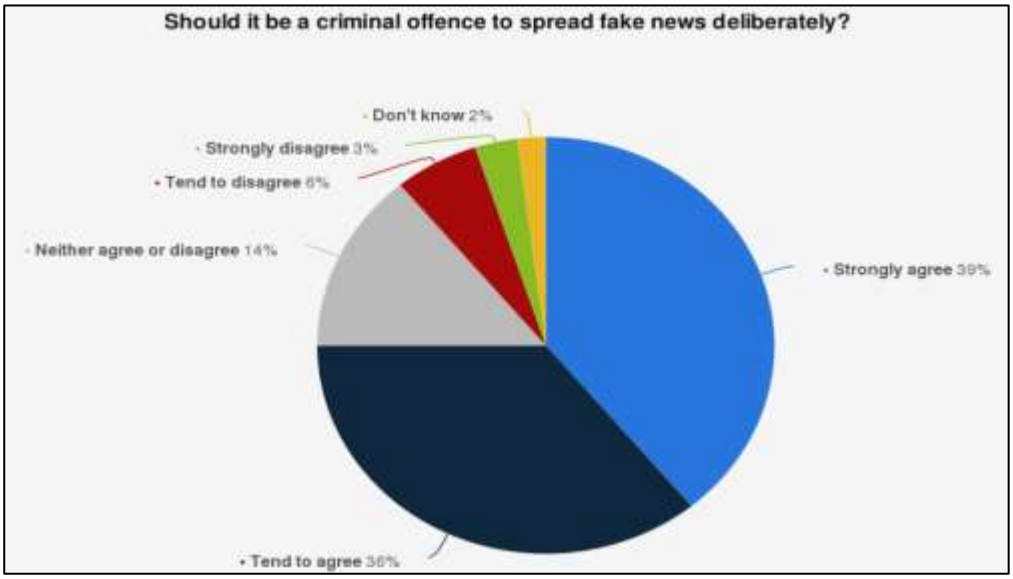

Figure 2.2.6. Consideration on whether deliberate release of fake news should be considered as a crime. Source: Ipsos MORI, King's College, London, 2019 © Statista.

However, it is not so clear on the role of administrations in the control of fake news, as the respondents considered that there may be a risk of political bias.

Table 2.2.2

Answer to the question «Which of the following institutions and media actors should act to stop the spread of 'fake news'?». (Max. 3 answers).

	Journalists	National authorities	Press and broadcasting management	Citizens themselves	Online social networks	EU institutions	Non-governmental organisations	Others (SPONTANEOUS)	All of them (SPONTANEOUS)	None (SPONTANEOUS)	Don't know
UE28	45	39	36	32	26	21	15	1	4	1	4
Sex											
Male	44	40	34	32	24	23	17	1	4	2	3
Female	45	38	38	32	27	20	13	1	5	1	5
Age											
15-24	48	35	37	39	39	19	17	0	5	1	1
25-39	48	37	40	34	31	22	16	1	4	1	2
40-54	45	41	38	33	25	22	14	1	4	1	3
55 +	42	39	32	29	18	21	14	2	4	2	7
Education (End of)											
15-	38	34	28	27	20	18	10	2	4	3	9
16-19	44	39	36	30	28	20	16	1	4	1	5
20+	47	40	39	34	24	24	15	1	4	1	3
Still studying	46	38	36	41	38	19	17	0	5	1	1
Respondent occupation scale											
Self-employed	46	34	34	35	24	21	17	1	4	2	3
Employee	48	41	41	34	30	23	16	1	5	1	2
Manual workers	40	34	35	32	26	18	14	2	4	1	5
Not working	43	39	33	30	23	21	14	1	4	2	6
Frequency of Online Social Media use											
Every day or almost everyday	47	39	39	34	31	22	15	1	4	1	2
At least once a week	45	39	36	36	27	25	16	1	4	1	3
Several times a month	47	36	39	29	26	18	17	1	6	3	4
Seldom or never	42	37	32	30	18	20	15	2	4	2	8
Exposure to Fake News											
Every day or almost everyday	46	40	36	35	24	22	16	1	5	1	2
At least once a week	46	40	40	34	29	22	16	1	4	1	3
Several times a month	46	38	40	32	26	20	14	1	5	1	4
Seldom or never	42	36	30	27	25	21	13	2	3	2	8

Base: All Respondents (N=26,576)

Note. Source: Flash Eurobarometer 464, 2018 (European Commission, 2018)

By the end of 2020, the vaccine against COVID-19 began to be used. However, on analysing the social attitude, disinformation and fear has permeated society giving rise to doubts. A recent (April 2021) example is the reluctance to use the Astra Zeneca vaccine even when the risks of thrombosis have not been totally clarified and despite the European Medicines Agency (EMA) concluding that the benefits outweigh the risks of rare cases of blood clot platelets (Østergaard et al., 2021)

As reported by the *Centro de Investigaciones Sociológicas* [Centre of Sociological Investigation] of Spain (CIS), the percentage of reluctance for vaccination increased during the last months of 2020.

Table 2.2.3

Willingness to get COVID-19 vaccination.

	Yes	No	NA
September	44.4	40.3	15.3
October	40.2	43.8	16.0
November	36.8	47.0	16.2
December	32.5	55.2	12.3

Note. Source: CIS (Centro de Investigaciones Sociológicas, 2020)

Table 2.2.4

Willingness to get COVID-19 vaccination by ages (December 2020).

	TOTAL	Sexo de la persona entrevistada		Edad de la persona entrevistada					
		Hombre	Mujer	De 18 a 24 años	De 25 a 34 años	De 35 a 44 años	De 45 a 54 años	De 55 a 64 años	65 y más años
Estaría dispuesto/a a vacunarse inmediatamente	32,5	39,3	26,3	20,9	23,9	27,6	32,9	38,8	38,9
Preferiría esperar a conocer los efectos	55,2	49,2	60,7	72,3	61,0	59,2	56,6	50,8	46,9
No estaría dispuesto/a a vacunarse en ningún caso	8,4	8,3	8,5	3,4	13,5	11,7	7,0	7,3	6,8
N.S.	3,5	2,8	4,1	2,7	1,2	1,5	3,3	2,5	7,1
N.C.	0,3	0,4	0,3	0,7	0,4	-	0,2	0,6	0,4
(N)	(2.131)	(1.018)	(1.113)	(148)	(259)	(392)	(426)	(358)	(545)

Note. Source: CIS (Centro de Investigaciones Sociológicas, 2020)

The trend reversed with the availability of the first vaccines.[3]

[3] See: *https://news.gallup.com/poll/327425/willingness-covid-vaccine-ticks.aspx (accessed on 21 April 2021).*

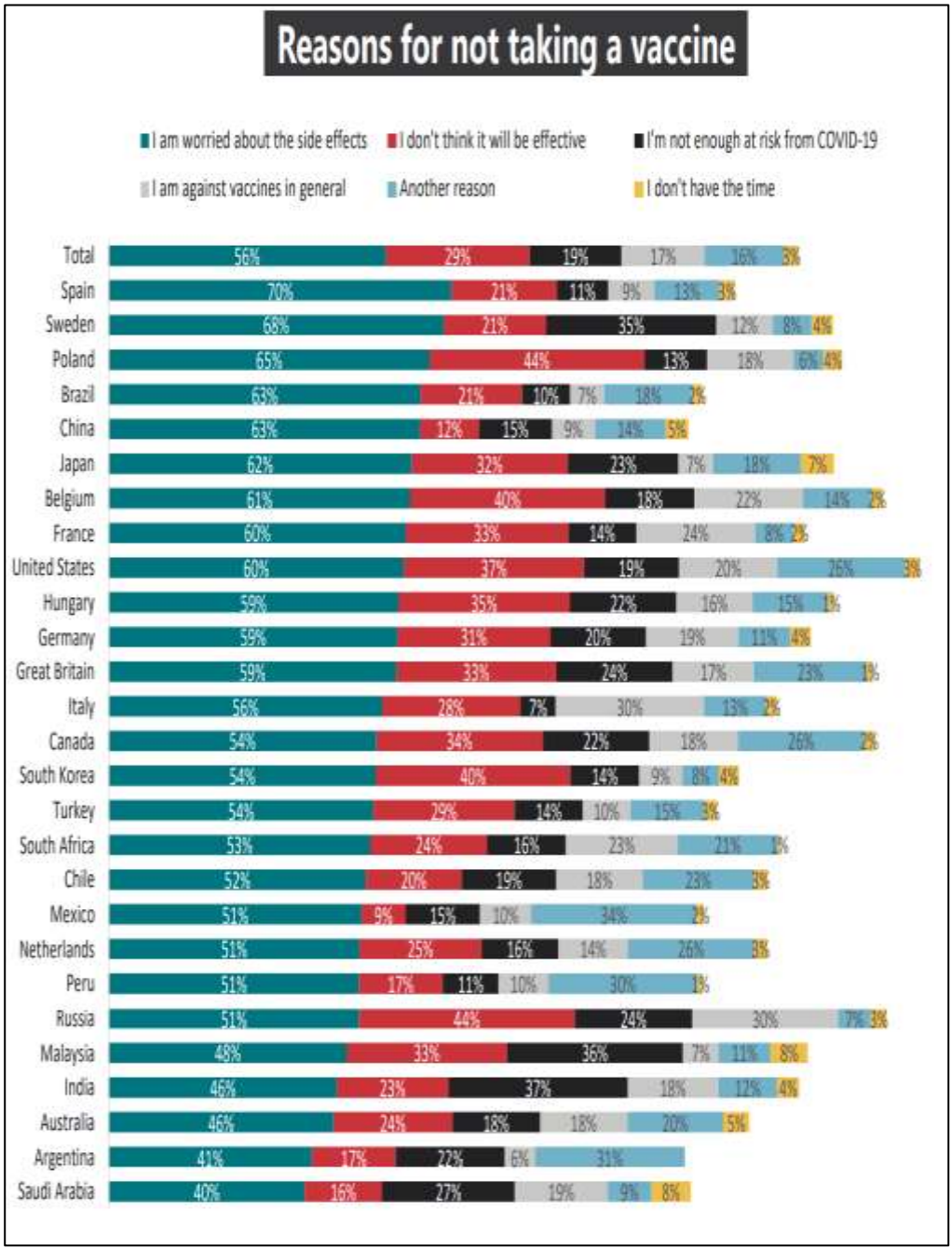

Figure 2.2.7. Reasons for not accepting vaccination against COVID. 19. Source: Ipsos Survey for the World Economic Forum (Global Advisor, June 24 – August 7, 2020) (IPSOS, 2020).

Thus, the questions addressed in this paper were:

1/ Is it possible within the Spanish legal framework to establish mandatory vaccination against COVID-19?

2/ Should the administration take an active, leading role in fighting against fake news?

3/ Is there is a way to achieve more control and regulation of fake news released by physicians and other health care professionals who are obliged to follow an ethical code?

2.2.2. Paper II text. Author's version format.

COVID-19, Fake News, and Vaccines: Should Regulation Be Implemented?

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Abstract

We analysed issues concerning the establishment of compulsory vaccination against COVID-19, as well as the role of misinformation as a disincentive—especially when published by health professionals—and citizen acceptance of measures in this regard. Data from different surveys revealed a high degree of hesitation rather than outright opposition to vaccines. The most frequent complaint related to the COVID-19 vaccination was the fear of side effects. Within the Spanish and European legislative framework, both compulsory vaccination and government regulation of FN (Fake News) appear to be feasible options, counting on sufficient legal support, which could be reinforced by additional amendment. However, following current trends of good governance, policymakers must have public legitimation. Rather than compulsory COVID-19 vaccination, an approach based on education and truthful information, persuading the population of the benefits of a vaccine on a voluntary basis, is recommended. Disagreements between health professionals are positive, but they should be resolved following good practice and the procedures of the code of ethics. Furthermore, citizens do not support the involvement of government authorities in the direct control of news. Collaboration with the media and other organizations should be used instead.

Keywords: COVID-19; vaccination; fake news; medical code of ethics; governmental regulations.

1. Introduction

With the appearance of vaccines against COVID-19, it is worth asking whether their administration should be maintained as voluntary, which in turn raises the question of to what extent individual freedom can and should prevail over the common social good. On the one hand, this is a question that is rooted in community values (for example, in the USA, the value of the sovereignty and total autonomy of the individual is strongly rooted) and on the other, the concept of public health and the measures and institutions that are needed to take care of it, necessitating an analysis of how to make the corresponding regulations compatible with the individual values described.

The situation that arose after the outbreak of COVID-19, with lockdown measures and extra time for the generation, circulation, and reading of all kind of news, has been the perfect breeding ground for the development of denialist positions, conspiracy theories, and fake

news (FN), which have sown turmoil in a part of the population that is facing a change of the social paradigm set after the Second World War and that seemed immutable.

The issue is particularly critical when misinformation or opinions that go against the flow of evidence-based information are publicized by expert professionals, as opinions of scientists, doctors, other health experts are generally considered very trustworthy [1,2,3].

However, political action must be based on good global governance, and good governance requires public legitimacy [4,5,6], something that is complicated when negative attitudes without a scientific basis become widespread and are even promoted by some health professionals.

This paper overviews the issue of compulsory vaccination when faced with misinformation concerning COVID-19, FN, and myths related to vaccination, with particular emphasis on those publicized by healthcare professionals or experts, analysing the legal bases for eventual regulatory control and its acceptance by citizens.

2. Materials and Methods

Following the legal reasoning (comprehensive *Juristischen Methodenlehre*) [7,8] we analyse the autonomy of the individual and the freedom of information as essential elements of the freedom of expression, the fundamental, human, and conventional rights versus the compulsory introduction of the COVID-19 vaccine, and the possible regulation of published news. Public opinion input, as promoted by the Organisation for Economic Co-operation and Development (OECD/OCDE) and the EU [9], has been obtained as part of the current request for evidence in the good governance approach for policymakers [4,5,6,10,11].

Citizens' opinions, from different surveys and countries related to FN in general and to COVID-19 in particular, have been obtained and processed (grouping and proportional computing [12]), after being collected through Statista® (Statista GmbH, Hamburg, Germany) [13]. Specific information for the EU, including the Flash Eurobarometer 464, has also been used to gather information [14]. Earlier references include the report for the European Commission (State of vaccine confidence in the EU) [15] and the IPSOS survey for the World Economic Forum on vaccination to prevent COVID-19 [16]. The latest data on voluntary vaccination intentions in Spain come from the Centre for Sociological Research of Spain (CIS) [17], and from the Invymark Institute, as presented in the two newscasts on the television channel *La Sexta* on 28 November 2020.

Recent documents and regulations from the EU and Spain have also been analysed, including information provided at the webinar (University of Salamanca, 26 November 2020) *El Procedimiento de actuación contra la desinformación en la defensa del Estado de Derecho* (Procedure for action against disinformation in defence of the rule of law) by the Director of the Department of National Security of the Presidency of the Government.

3. Results

The legal analysis will be commented on in the discussion section. Public opinions related to FN are summarized in **Figure 1**. Surveys suggest that citizens do not much trust in information from the media but feel reasonably confident in their capacity to distinguish fake news from real.

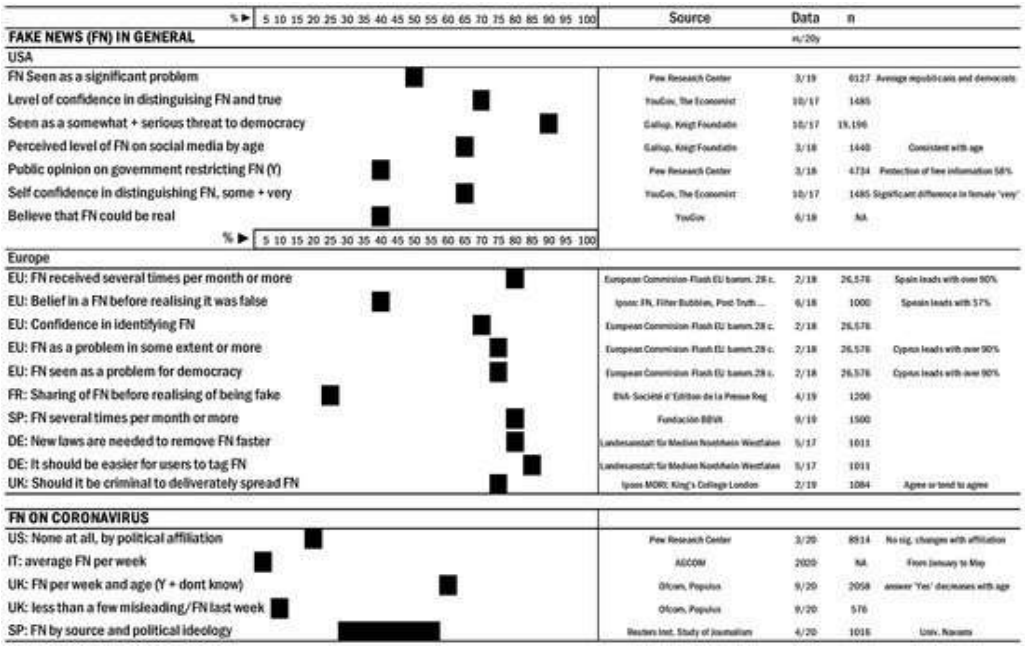

Figure 1. Summary of citizen opinion from different countries related to false news, including fakes on COVID-19. Source: Authors' computation from different surveys procured from the Statista database.

The most frequent complaint, related to vaccination against COVID-19, is fear of side effects [15,18], which raises the question of how safe and effective the vaccine should be, and the procedures to counteract this fear, mostly developed after the confusion of ideas resulting from the constant circulation of FN.

FN is considered a major problem in 68% (65 or older) to 80% (18 to 29 years old) of USA citizens, and somewhat of a threat or a serious threat to democracy in 88% (Knight Foundation Gallup) [19]. The perceived level of FN on social media in the USA, as of May 2018, is quite consistent over all age groups (about 63%). Social media sites are considered partly or mostly responsible for the spread of FN in 89% of the cases, with 69% considering that these social media sites are not doing enough to stop the spread of FN on their sites (Monmouth University) [20,21].

As for Europe and according to data from the Flash Eurobarometer as of February 2018 (n = 26,576), about 80% of the respondents encountered FN several times a month or more, with 37% of responses in the everyday/almost everyday group [14].

About 81% of Spaniards (2019) perceived FN "often" or "several times", with only 7% indicating almost never [22], meaning the great majority of the population is perceiving a significant amount of FN.

In Italy, the share of online FN related to coronavirus between January and May 2020 was about 5% per week, with Facebook recognized by almost 80% of those surveyed, regardless of age, as the primary social media in this regard [23,24].

In the UK (September 2020), 20–30% of respondents had encountered information/news about coronavirus that they thought was false or misleading in the previous week, with a similar number saying they did not know, leaving less than 50% declaring they were unaware of false information [25]. The pattern is consistent when analysed by age groups; 81% declared that received FN a few times a week or more, with 7% of them reporting ten or more times a day [25].

The issue of misinformation has become so critical that the World Health Organization (WHO) has dedicated a site specifically to reporting misinformation online [26]. The European Commission also recommends following the advice of public health authorities, and websites of relevant organizations. The European Centre for Disease Prevention and Control (ECDC) and the WHO work in close cooperation with online platforms [27,28,29]. There are also several funded projects for fighting against disinformation [30] and a permanent analysis by the Social Observatory for Disinformation and Social Media Analysis (SOMA) [31].

A 2018 EU survey on FN and disinformation online [14]—where up to three answers could be chosen from seven possible options—requested the opinion of respondents on who should act to stop the spread of FN. After mathematical processing of the resulting 224 points as relative percentages, they were included in four main groups: (1) mass media professionals plus administrators or media organizations, (2) governmental authorities either at a national or EU level, (3) citizens, and (4) non-governmental organizations + other, with the predominant option to stop FN being for the professionals to act themselves (**Figure 2**).

Figure 2. Who will stop fake news? (EU 2018). Source: Authors' mathematical computation of data from Flash Eurobarometer 464 [14].

In a 2018 a survey about vaccines with 28,782 respondents across the 28 EU member states, the perception towards vaccines was positive, with agreement (strongly or tend to agree) at 90%, safety at 82.8%, effectiveness at 87.8%, and compatible with religious beliefs at 78.5% [15]. The importance of vaccination was found to be related to the disease.

According to the IPSOS survey for the World Economic Forum (24 July to 7 August 2020), 74% of respondents agree (37%) or somewhat agree (37%) on the question as to whether they will get the vaccine when available. Forty percent thought they would not have the ability to get the vaccine by the end of 2020. Among the reasons for not getting vaccinated, 56% were worried about side effects, 29% think that it will not be effective, 19% that they are not enough at risk from COVID-19, and 17% are against vaccines in general [16].

The perceptions and intentions of the Spanish population regarding the COVID-19 vaccine have been analysed by the Centre of Sociological Investigation of Spain (CIS) on a regular basis. The number of respondents willing to be vaccinated fell from 44.4% in September to 32.5% in November, when 55.2% of overall respondents chose the option of waiting to see the side effects, but among those within the 18–24 age range, 72.3% of the cases preferred to wait [17]. Another survey from the Invymark Institute, during the week of 23 November, was broadcast by the television channel *La Sexta* (28 November 2020). Up to 61.6% among the groups surveyed do not believe that there will be effective vaccines in the coming months.

Almost half of the respondents are not willing to be vaccinated when the vaccine is available (a similar percentage as in the CIS survey), with the reasons being, firstly, that they prefer to wait a while (50.1%), secondly, concern about side effects (44.4%), and, thirdly, that they do not believe vaccines are efficient (4.6%). Although there are some variations of the percentages in relation to the IPSOS survey data related to Spain, a substantial amount of the respondents expressed a high degree of hesitance rather than outright opposition to vaccines.

The lack of confidence in prevention is also evident in the response to the question (Invymark Institute) on when the respondent believes that a certain normality will return. The majority response (48.6%) is two or more years, for 42.0% in one year, and 8.8% believe that normality will not return for many years.

4. Discussion

As has happened in other critical phases of history, a percentage of a disoriented population is vulnerable to the influence of gurus and prophets who reveal the errors of today's society and show alternative paths, alien to the official postulates. The spread of the SARS-CoV-2 virus is the perfect storm for the growth of conspiracies, flat-earthers, and such like.

The situation has significantly worsened since the COVID-19 pandemic included lockdowns, with resultingly more time spent on chatting and tweeting. A survey by the Reuters Institute for the Study of Journalism revealed that the percentage of the population that has found FN or misleading news related to coronavirus in Spain, as of April 2020, is quite consistent, even considering political ideology, although the data show a relevant increase in the percentage of right/far-right respondents' attribution to the National government or linked organizations. The Institute also recognizes that "journalists no longer control access to information, while greater reliance on social media and other platforms gives people access to a wider range of sources and "alternative facts", some of which are at odds with official advice, misleading, or simply false" [1].

At the present time, without effective antiviral treatment, social isolation and vaccination seem to be the most rational hope for fighting the pandemic. With this "RMS Titanic orchestra" social attitude briefly outlined; two key questions arise in this situation:

(1) Can the authorities implement these measures, for example, the vaccination of people who refuse it, even by use of force?

(2) Who (and how) should stop the publication of FN, particularly when this false news is published by registered health professionals, denying vaccination, and placing not only themselves at risk but the entire community? Is it legally and democratically founded to take coercive action against the desire of citizens and to act to curb the opinions of certain professionals who move outside the parameters of professional praxis?

Starting with this second point, in Spain, as in other developed countries, freedom of expression and the dissemination of news is a constitutional right (Art. 20 of Spanish Constitution [32]). Of even more importance, the constitutional text does not require the information to be true. This freedom is also supported by the European Convention on Human Rights (ECHR) (Art. 10) [33], although both texts establish limitations in relation to public safety (ECHR, Art. 10.2), the observance of the other rights recognized in Title I of the Spanish Constitution (Art. 39.1), and the protection of public health (Art. 43).

The problem of misinformation has grown to a point that the EU has promoted an in-depth analysis. "The legal framework to address 'fake news': possible policy actions at the EU level" [34] and reinforced responses in collaboration with the USA [35]. Furthermore, the EU is strengthening actions to tackle COVID-19 disinformation [36], as "in the EU and elsewhere, coordinated disinformation messaging seeks to frame vulnerable minorities as the cause of the pandemic and to fuel distrust in the ability of democratic institutions to deliver

effective responses" (EEAS special report on 1 April 2020, recently updated) [37]. The document also includes a taxonomy of the misinformation relating to the COVID-19 pandemic.

Although the initial efforts of both European and Member States' authorities were devoted to combating specific misinformation in order to ensure the transparency of electoral processes, the growth of FN and the subsequent erosion of institutions and the danger of polarization of the society that this entails have forced states to take measures, which in the case of Spain, have been specified in the Official Gazette of 5 November 2020, with Order PCM/1030/2020, of 30 October, which publishes the Procedure for Action Against Disinformation approved by the National Security Council [38].

This new regulation will allow the collaboration of the media in the fight against disinformation that may cause damage or affect fundamental rights, such as the right to health as enshrined in law. As for COVID-19 and cybercrime, according to the EU report: "Criminals use the pandemic to carry out various scams and attacks […]. Europol, the EU's law enforcement agency, collects information from EU member states and publishes regular reports on how criminals are adapting their crimes to exploit the coronavirus pandemic" [39].

As result of misinformation, a citizen may act (or omit to act) with dangerous consequences for him/herself or for third parties. This is even more the case when it refers to behaviour outside of the medical praxis related to the COVID-19 vaccine, under the influence of a publication of an (allegedly) qualified healthcare professional, given that, in Spain, scientists, doctors, and other health experts rank high in the degree of confidence in the information they publish [1].

The question of misinformation provided by medical professionals has two key aspects:

(1) There is freedom in receiving and publishing information about health, but this must also be reliable as required by standards of praxis and *lex artis ad hoc*. Freedom of information is an essential element of the fundamental right of freedom of expression, as recognized by Resolution 59 of the UN General Assembly adopted in 1946 [40], as well as by Article 19 of the Universal Declaration of Human Rights (1948) [41]. According to the World Medical Association Declaration of Geneva (1948), medical knowledge cannot be used to violate human rights and civil liberties, even under threat [42].

The right to have proper information relating to health is also recognized in the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine (Oviedo, 4 April 1997) [43].

The information provided by Spanish physicians must be understandable and true (Art. 4.2) of Law 41/2002, establishing the basic regulation of patient autonomy and of rights and obligations regarding clinical information and documentation. Additionally, in Art. 6., they "have the right to know about the health problems of the community when these involve a risk to public […]" [44]. This is a derivative of the human rights recognized in international treaties and the Spanish Constitution (health protection (Art. 43) and education of consumers and users (Art. 51)) [32].

(2) The practice of medicine is a regulated activity. It is subject to compulsory membership of an Official Medical Association (*Colegio Médico Oficial*) and compliance with its rules and procedures, mainly the ethical code [45]. The medical association can initiate disciplinary proceedings (Art. 44.4) and impose the sanctions regulated in the General Statutes of the Medical Association (Art. 2).

The code of ethics establishes in Art. 7 that "a medical act is understood to be any lawful activity carried out by a legitimately qualified medical professional, whether in the field of care, teaching, research, expertise, or others […]" Therefore, the release of information is included in this concept. A number of other articles in this code focus on avoiding the imposition of their own convictions (Art. 9.1), assuming the negative consequences of their actions

and errors, offering a clear, honest, constructive, and adequate explanation (Art. 17.1), providing assistance of human and scientific quality (Art. 21.1), refraining from actions that exceed their capacity (Art. 22), and avoiding "practices inspired by charlatanism, those with no scientific basis and which promise patients a cure, and those illusory or insufficiently proven procedures proposed as effective" (Art. 26.2). In addition to the obligation for information to be rigorous, it must be transmitted through the appropriate channels (Art 37.3). Public controversy shall be avoided; disagreements shall be resolved at the professional or associate level (Art. 38). The physician shall not participate in any activity that involves manipulation or hiding of information (Art. 59.4). Art. 64.3 establishes actions as contrary to deontology: "(a) making known in a premature or sensationalist way procedures of efficacy that have not yet been demonstrated or exaggerating this […] (g) Advertising or promoting a product without sufficient scientific support or with insufficient information about it". Additionally, Art. 65.3: "medical advertising must be objective, prudent, and truthful, so that it does not raise false hopes or spread unfounded concepts".

In summary, as has been repeatedly stated in case law [46], the physician is not responsible for the outcome, but for performing his or her professional duties in accordance with good practice and *lex artis ad hoc* and this includes the dissemination of only true scientific information through the appropriate channels, and never sowing confusion, covering up, or disguising criticism of other professionals or their work and results.

Consequently, there are legal procedures for the prosecution of professionals who spread FN that can potentially affect health. In addition to the procedures established by the Medical Association, there may also be civil and even criminal proceedings against misinformation provided by healthcare professionals. If it is a result of a contractual relationship between the physician and the client, the Civil Code (Art. 1101) may be of application: "those who, in the fulfilment of their obligations, are guilty of fraudulent, negligent, or delayed action, and those who in any way contravene these obligations, shall be liable for compensation". If the FN is broadcast free of charge by the health professional and a contractual relationship between him/her and the recipient cannot be invoked, there may still be a proceeding based on Article 1902 of the Civil Code: "the one who, by action or omission, causes damage to another, intervening guilt or negligence, is obliged to repair the damage caused".

However, it is understandable that given the speed of the development of COVID-19 news, the flourishing of FN may have permeated even to professionals, but it is a must that information publicized by them be evidence based and supported by scientific evidence. These professionals have obligations under the code of ethics and run the risk of being subject to legal actions for non-compliance with the good practices of *lex artis ad hoc.*

Regarding the option of compulsory vaccination, we must look at how this could be achieved. It could be based on the following rationale.

In Spain, Organic Law 3/1986, of 14 April, on Special Measures in the Field of Public Health [47] Article 2, states: "the corresponding health authorities may take measures for examination, treatment, hospitalization, or control when there is reasonable evidence to suggest that the health of the population is endangered by the particular health status of a person or group of persons or by the health conditions in which an activity is carried out" and also Law 41/2002, of 14 November, specifies the basic regulation of patient autonomy and of rights and obligations regarding clinical information and documentation [44] in Article 9.2: " (a) when there is a risk to public health due to health reasons established by law." The legal support may be increased by a specific amendment concerning the possibility of introducing a vaccine or compulsory treatments when there may be beneficial effects for all citizens, such as in a pandemic or similar.

Compulsory vaccine regulation would pass the proportionality test as required by the international agreements signed by states in the European Convention on Human Rights [33],

since Article 8.2 states: "There shall be no interference by a public authority with the exercise of this right except such as is in accordance with the law and is necessary in a democratic society in the interests of national security or public safety […]" In the case of opposition for religious reasons, in concordance with Art 9.2: "Freedom to manifest one's religion or beliefs shall be subject only to such limitations as are prescribed by law and are necessary in a democratic society in the interests of public safety, for the protection of public order, health, or morals, or for the protection of the rights and freedoms of others". For emergency situations, Article 15 could be also applicable: "Derogation in time of emergency: in time of war or other public emergency threatening the life of the nation, any high contracting party may take measures derogating from its obligations under this convention to the extent strictly required by the exigencies of the situation, provided that such measures are not inconsistent with its other obligations under international law".

In the Charter of Fundamental Rights of the European Union (2000/C 364/01) [48], compatibility may be found in Article 7, in Article 24 when the risk could affect children, and in Article 35 related to health protection.

However, should the vaccine be mandatory? In in a country with an advanced democratic system, the freedom and independence of the citizen to decide (agency, autonomy) is fundamental. Compulsory vaccination would create several grey areas and issues, starting with what a compulsory vaccine is, and issues such as what to do in the case of a person refusing mandatory vaccination, but offering instead to become isolated at home without external contacts. Moreover, a compulsory vaccination mandate would require, to be legally sustained, backing by extensive studies, including all age groups and diffusion of the scientific information prior to becoming part of the medical *praxis and lex artis ad hoc*, in addition to passing the proportionality test, as has been done with lockdown parity argument. Compulsory vaccination, according to good governance, requires the support of citizens, something that is hard to obtain at this point [4,5,6,9,10,11].

It seems that currently the only reasonable approach to COVID-19 vaccination is to promote it as a civic duty, rather than to establish mandatory treatment and penalties for not vaccinating. Adherence could be implemented with vaccine requirements in certain cases, such as for certain jobs in the public sector with frequent contact with the public (e.g., public employees, healthcare workers, police, food handlers, etc.), or as part of the requirements for admission to other work or travel.

In addition to the individual health benefits described, there are other potential externalities associated with a successful vaccination program, including benefits to the economy (avoiding productivity losses), and in avoiding the cost of delayed assistance for other diseases, the publicizing of which may help to increase adherence to vaccination [49].

5. Conclusions

Firstly, to obtain gains in health and costs, it is necessary to ensure that the COVID-19 vaccine is safe, without significant side effects, and with a durable immunity effect; however, confidence in the vaccine seems to be jeopardized by disinformation. Scientific data, rigorously analysed by prestigious professionals, must be disseminated to counterbalance the numerous hoaxes circulating in the media and social networks. Full information (together with the active collaboration of citizens) is not only a right but remains the first and cornerstone active measure in promoting a safe vaccination process to provide immunity to the community, including providing the latest scientific results to health professionals as a key element in the diffusion of true data. The relatively low perceived risk for COVID-19 is also another element in the reluctance to be vaccinated [23,50,51,52]. There are also additional approaches for psychological management and resilience, sometimes by novel means such as spot advertising [53], which open up possibilities for behavioural science approaches to the analysis of motivations and their management [54,55,56].

Secondly, for FN itself, following the information gathered from surveys [14], the main role in stopping it, according to the good governance approach, is not for governmental authorities, although new advances in legislation favour collaboration with the media. There is even a small percentage of respondents who consider FN as a right. However, FN can lead to life-threatening behaviours and, therefore, joint action is needed to keep freedom of information, while, at the same time, preserving health. The development of new tools is urgently needed. These could include deep learning techniques and natural language processing, developing systems easily integrated into internet browsers and social networks and providing immediate evidence of whether that statement, news, or content is true or possible misinformation and generating a sort of identifier (possibly in a similar way as the "likes") on the veracity of the information and its risk for health, or any other method to maintain the right of expression without endangering public health. In any case, the problem is complex and will require finding solutions that both respect freedom of information and guarantee health. A systematic control of information only by the government runs the risk of political bias and it is not the option preferred by citizens, as expressed in surveys.

Thirdly, the case of FN spread by registered professionals (RNs, MDs, etc.) is particularly critical, as, according to the surveys, the news publicized by professionals is considered as highly trustworthy. Users are increasingly looking for health information in the media, and the media is seen as a way of providing information to be promoted by medical associations [3]. New regulations, probably through professional associations, may be required to enhance compliance with the code of ethics, in case of news going against medical praxis, published by associated health professionals.

However, again, prior to promoting punitive actions and the active circulation and updating of scientific data, training and evidence-based continuous education among the professionals promoted by the Medical Association, universities, and other academic institutions seem a reasonable first step.

In conclusion, although, in extreme circumstances, there may be legal possibilities for the compulsory administration of vaccines and for fighting against misinformation when it could undermine public health, particularly when promoted by healthcare professionals, rather than direct and exclusive administrative action, the options preferred by citizens, as expressed in surveys, seem to be for proactive and educative actions of promotion of COVID-19 vaccination as the citizens' duty, and fighting against FN through information and collaborative plans at governmental level, associations, and media, taking advantage of a the new legal framework [38].

Author Contributions

Conceptualization and methodology, J.E.M.-F.; software, J.E.M.-F.; validation, P.P.-B. and D.V.-C.; formal analysis, P.P.-B.; investigation, J.E.M.-F. and D.V.-O.; resources, D.V.-O.; data curation, D.V.-O.; writing—original draft preparation, J.E.M.-F.; writing—review and editing, S.G.-d.-J.; visualization, S.G.-d.-J.; supervision, D.V.-C. and P.P.-B.; project administration, D.V.-C.; funding acquisition, Vivas Consuelo D. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest

The authors declare no conflict of interest.

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2.2.3. Comments to paper II.

Just when publicising and vaccination plans were starting, this paper analysed the impact of misinformation and the legal possibility of making the vaccine compulsory. The concern about the impact of fake news on health plans related to COVID-19 is notable and has generated responses from organisations outside the EU, such as WHO, as well as from the EU itself. In Spain, the possibility for the government to act has been reinforced by a new legal framework (National Security Council Order PCM/1030/2020, of 30 October; «BOE» no. 292, of 5 November 2020, publishing the Procedure for Action Against Disinformation approved by the National Security Council, 2020; pp. 91912–91919). The case of disinformation is particularly serious when health professionals spread doubts about vaccination against COVID-19, as their opinions are considered as highly trustworthy according to survey.

Taken from different sources, the paper analysed data concerning confidence in vaccines (European Commission, 2018) prior to the coronavirus pandemic, and whether this confidence had changed following the appearance of SARS-CoV-2. It used the information provided by the World Economic Forum (IPSOS, 2020), and the Spanish Centre for Sociological Research, (Centro de Investigaciones Sociológicas [Centre of sociological investigations], 2020). As reported in the paper, there is no significant outright rejection of the vaccines, although it is true that disinformation has been significant and has impacted with a progressive fear of side effects.

In view of this situation, the paper examines whether it is possible to establish a legal framework to compel vaccination, and whether government regulation can be imposed on fake news. To gauge public opinion, various databases have been analysed, with the macro database ® Statista proving to be very useful for this purpose.

As a result of this analysis of trends and opinions, and counting with expert legal assistance, a possible way to establish the legal obligation to vaccinate was found. However, its compulsory implementation has many gaps and unresolved issues and would not be well received by the public. Therefore, it has been suggested that it should remain voluntary, appealing to the solidarity and responsibility of citizens (which can be stimulated by appropriate campaigns to disseminate accurate information).

Regarding fake news, the situation is worrying, since some health professionals —who are obliged to follow a code of ethics, given that to practice medicine in Spain it is necessary to be a member of a Medical Association (*Colegio Oficial de Médicos*) and this implies acceptance of the code of ethics— disseminate information under their name and report themselves as medical professionals, which is outside the standards of good *praxis and lex artis ad hoc*. This is especially worrying because, as indicated above, the opinions of health professionals are highly accepted in society.

Disagreements between health professionals are positive, but they must be resolved at the level of the scientific community, avoiding the dissemination of unverified information, following good practice and the procedures of the code of ethics. However, again, it seems premature to establish a criminal procedure for this purpose.

The rationale based on the survey reviewed seems to favour first exhausting the current regulations and only in cases of reiteration and a clearly dangerous attitude on the part of the health professional who disseminated false news would a civil or criminal complaint be initiated. This more permissive and tolerant approach is supported by survey analyses in which respondents fear the possibility of deviation towards particular political interests if decisions are left to the authorities.

2.2.4. Congress presentation: Covid-19 and school-age vaccination.

A further view on the question of COVID-19 vaccination but focused on children and pregnant women was presented in Spanish in the paper «COVID-19 and School-Age

Vaccination», at the VI International Virtual Congress on Education in the 21st Century (14–28 April 2021), a meeting under the general theme on effects of COVID-19.

The review resulted in highlighting the impact on education of stay-at-home policies in the COVID-19 pandemic, which transcends the apparent difficulties of distance learning and the unrest generated in the home environment. According to some estimates, school closures averaging 14 weeks in 2020, reported by the United Nations Educational, Scientific and Cultural Organisation (UNESCO, 2021), could represent more than a 1% loss of future income. The economic impact could last for decades. Face-to-face activity in the early stages of education is crucial and the consequences of school closures can persist for years.

Based on data from Burguess and Sievertsen, it has been estimated that it results in a standard deviation of 1% of learning indicators for every 10 days of schooling lost, so that if applied to the 14-week average closure as reported by UNESCO, this would result in a deviation of 9.8%, which in wage terms would represent a loss of more than 1% of future earnings (Burguess & Sievertsen, 2020; Sainz & Sanz, 2020).

The British Royal Society has suggested, considering data from various studies and the DELVE report, that school time lost due to the pandemic could harm the UK economy for the next 65 years. The data has had a huge echo in the media and in the Confederation of School Trusts (Royal Society, 2020).

Assuming, in accordance with the expert committees in clinical ethics, that a single prioritization cannot be established in the vaccination programs against COVID-19, it would then be possible to include the option of preference by life cycle, which would give priority to the child population (Branswell, 2020; Bubar et al., 2021; Giubilini et al., 2020; Gupta & Morain, 2020). An overview of the different vaccination strategies reported in the scientific literature against COVID-19, concluded that: 1/ there is evidence that vaccination plans based on consensus and informed consent may be sufficient to promote voluntary vaccination even in pregnancy and paediatric age, implemented by a rigorous information campaign; 2/ the option of life-cycle preference, giving priority to the paediatric population, would be very cost-effective and should be incorporated as a priority strategy in vaccination plans. Prioritizing the child population in a vaccination plan would have effects that go far beyond those that can be deduced from the COVID-19 child morbidity and mortality data. In conclusion, the paper postulates that vaccination plans, through the provision of consistent, rigorous and non-partisan information, in consensus and with informed consent, can be extended to pregnancy and paediatric age (Kamidani et al., 2021; Mayo Clinic, 2020).

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2.3. PAPER III (2021). Simplified Mathematical Modelling of Uncertainty: Cost-Effectiveness of COVID-19 Vaccines in Spain

2.3.1. Introduction to paper III.

This paper introduces a simplified model for estimation of cost-effectiveness. It was based on information on two dates, 27 October 2020 and 17 February 2021, a period with an active outbreak. The paper was focused on three main aspects:

Firstly, comparatively analysing the approximately six-month interval from the start of the pandemic of COVID-19 in Spain as compared with influenza. It was considered convenient to compare these two diseases as it was considered, and so declared by some public authorities, that COVID-19 was no more than another influenza outbreak.

Secondly, providing an early approach to the direct costs that the pandemic is originating in the Spanish healthcare system. Again, the CMBD for COVID-19 was not yet available, but there are reports on admissions and the cost of similar services has been published based on case-mix and supported by other publications specifically reporting COVID-19 hospitalisations. A range of costs was provided. The model, as in paper one, is based strongly on mortality as a reliable variable, a data that is usually consistent, and may be obtained from alternative sources, such as death registers, cemeteries, etc.

Thirdly, presenting a first estimation of cost-effectiveness of the vaccine, something really approximative, as when the paper was written there was an active outbreak of the coronavirus in Spain and there was still no clear information about vaccine prices; furthermore, there were comments in the media about the possibility of caritative provision of the vaccine to certain regions. Additionally, it started to become evident that there were different variants of the virus, and neither their evolution nor their pattern of population involvement was known. The model was planned as *ceteris paribus*.

For hospital information on age, the sources offer data by decades (0–9, 10–19, …90+). The median of each age band was included in the calculation and then the average of medians was computed if needed.

In the paper the life table was presented in extract (range ages for each five years) but yearly information was used as shown in the table 2.3.1 below. Intermediate values were estimated by linear interpolation.

In summary, the idea has been to provide a simple (static) model with two ‘snapshots’ for a first approach to a cost-effectiveness figure, a value evidently in constant change. For example, by applying the model to the two dates (October 27 and February 17), there is a difference of about 41% change in the ICER value, indicating the importance of QALYs lost with the pandemic.
Therefore, rather than the figures themselves, it is important that the model allows estimates based on the mortality rate only and the other variables are derived mathematically.

Table 2.3.1

Life table with utility ratios (U_i) used in the publication.

Men♦Age	Life expectancy	U	LE good health	Women♦Age	Life expectancy (	U	LE good health
0	80.48	0.793623	63.87	0	85.9	0.79350	68.13
50	31.85	0.687555	21.90	50	36.8	0.60030	22.10
51	30.95	0.684928	21.20	51	35.9	0.59802	21.45
52	30.05	0.682301	20.50	52	34.9	0.59575	20.81
53	29.17	0.679673	19.82	53	34.0	0.59348	20.18
54	28.29	0.677046	19.15	54	33.1	0.58171	19.24
55	27.42	0.674419	18.49	55	32.2	0.56993	18.32
56	26.56	0.659363	17.51	56	31.2	0.55816	17.43
57	25.70	0.644307	16.56	57	30.3	0.54639	16.56
58	24.86	0.629250	15.64	58	29.4	0.54211	15.94
59	24.03	0.614194	14.76	59	28.5	0.53782	15.32
60	23.20	0.599138	13.90	60	27.6	0.53354	14.71
61	22.39	0.597259	13.37	61	26.7	0.52925	14.12
62	21.58	0.595380	12.85	62	25.8	0.52497	13.53
63	20.78	0.593502	12.33	63	24.9	0.51026	12.69
64	19.99	0.591623	11.83	64	24.0	0.49556	11.88
65	19.21	0.589744	11.33	65	23.1	0.48085	11.10
66	18.43	0.583002	10.75	66	22.2	0.47939	10.64
67	17.66	0.576260	10.18	67	21.3	0.47792	10.18
68	16.91	0.569518	9.63	68	20.4	0.47646	9.73
69	16.16	0.562776	9.10	69	19.5	0.47500	9.29
70	15.43	0.556034	8.58	70	18.7	0.47353	8.85
71	14.70	0.549374	8.07	71	17.8	0.47207	8.41
72	13.98	0.542715	7.59	72	17.0	0.47061	7.99
73	13.28	0.536055	7.12	73	16.1	0.46914	7.57
74	12.59	0.529396	6.66	74	15.3	0.46768	7.15
75	11.91	0.522736	6.23	75	14.5	0.46622	6.75
76	11.25	0.516076	5.81	76	13.7	0.44798	6.13
77	10.61	0.499435	5.30	77	12.9	0.42975	5.54
78	9.99	0.492775	4.92	78	12.1	0.41151	4.99
79	9.39	0.491107	4.61	79	11.4	0.39328	4.47
80	8.80	0.489438	4.31	80	10.6	0.37504	3.99
81	8.24	0.487581	4.02	81	9.9	0.35681	3.55
82	7.70	0.480155	3.70	82	9.3	0.33857	3.14
83	7.20	0.478298	3.44	83	8.6	0.32034	2.76
84	6.71	0.462800	3.11	84	8.0	0.30211	2.42
85	6.25	0.456140	2.85	85	7.4	0.28387	2.11
86	5.82	0.441656	2.57	86	6.9	0.25008	1.72
87	5.42	0.427173	2.31	87	6.4	0.21629	1.38
88	5.04	0.412689	2.08	88	5.9	0.18250	1.08
89	4.71	0.398205	1.87	89	5.5	0.14870	0.81
90	4.39	0.383721	1.68	90	5.0	0.11491	0.58

Note. Source Authors' computation with data from INE and Eurostat databases.

2.3.2. Paper III text. Author's version format.

Simplified mathematical modelling of uncertainty: cost-effectiveness of COVID-19 vaccines in Spain.

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Abstract: When exceptional situations, such as the COVID-19 pandemic, arise and reliable data is not available at decision-making times, estimation using mathematical models can provide a reasonable reckoning for health planning. We present a simplified model (static but with two-time references) for estimating the cost-effectiveness of the COVID-19 vaccine. A simplified model provides a quick assessment of the upper bound of cost-effectiveness, as we illustrate with data from Spain, and allows for easy comparisons between countries. It may also provide useful comparisons among different vaccines at the marketplace, from the perspective of the buyer. From the analysis of this information, key epidemiological figures, and costs of the disease for Spain have been estimated, based on mortality. The fatality rate is robust data that can alternatively be obtained from death registers, funeral homes, cemeteries, and crematoria. Our model estimates the incremental cost-effectiveness ratio (ICER) to be 5132 € (4926–5276) as of 17 February 2021, based on the following assumptions/inputs: An estimated cost of 30 euros per dose (plus transport, storing, and administration), two doses per person, efficacy of 70% and coverage of 70% of the population. Even considering the possibility of some bias, this simplified model provides confirmation that vaccination against COVID-19 is highly cost-effective.

Keywords: COVID-19 vaccination; mathematical modelling; health economics modelling; Best Adjustment of Related Values (BARV); Cost-Effectiveness Analysis (CEA); coronavirus; healthcare expenditures; Quality Adjusted Life Years (QALY); Incremental Cost Effectiveness Ratio (ICER); collective choice; discount rate

1.Introduction

Since the first publications of efficacy data on COVID-19 vaccines [1,2], a growing number of other products have been developed in different countries by a number of pharmaceutical companies. However, it is crucial that a steady and adequate supply is available to the population within a short period of time. The COVID-19 pandemic has already imposed significant costs on national economies, causing increasing pressures on health budgets. Despite the effort it represents, it is essential that sufficient financial resources are guaranteed to carry out the vaccination plans. In this study, a mathematical model for cost-effectiveness analysis of COVID-19 vaccination is presented to pro-vide policymakers with the evidence of the economic value of this health intervention. It is worth noting that the absence of reliable data, and even more so, data in constant progression, make this estimation very difficult, especially in the context of a pandemic, when the time available for producing complex forecasts is limited, and health managers may not have sophisticated mathematical technology at their disposal. Simple mathematical model could provide an approach throw and some light on this issue [3], and the method and conclusions of this study can help facilitate setting priorities in the decision-making process and the allocation of the health care budget.

In addition to the proposal for the mathematical procedure, this document has three purposes. Firstly, to present some figures on the impact of COVID-19 on health, in support of the concept of serious disease, the control of which still requires additional economic efforts. To this end, the number of quality-adjusted life-years (QALYs) lost to the pandemic has been calculated; secondly, to establish an estimate of the cost of health care due to COVID-19 in Spain; and thirdly, to present data on the cost-effectiveness of the vaccine.

2. Materials and Methods

Data for Spain related to the situation of the COVID-19 pandemic on 27 October 2020 and on 17 February 2021 have been calculated using the Best Adjustment of Related Values (BARV) method, which attempts to adjust reliable figures within a range and calculate other less reliable but related values by means of an iterative adjustment, so that the possible errors of all the variables are minimized by minimizing all deviations [4]. Although a more complex computerized procedure may be used, results may also be obtained using a simple spreadsheet, with the possibility of adding weighting to more reliable data and by an iteration process obtaining the results for the less known variables that minimize all errors.

For mortality, the procedure already used in previous work [4] was followed, collecting the unexpected increase in mortality (excess deaths) registered in four periods from the Spanish Mortality Database (MoMo) [5], assuming (ceteris paribus) the increase to be due to COVID-19.

The QALY, $Q(x_A)$, representing the number of years (adjusted for quality) for each group of median age (A) lost as a result of morbidity/mortality due to COVID-19, have been calculated, based on the estimate of years of life expectancy (LE = x) for age A, using the formula [6,7]:

$$Q_0 = QALY(x_A) = \sum_{j=1}^{x_A} U_j (1-r)^{j-1}$$

Following Attema et al. [8], the utility U for each year obtained from the life table is discounted for the successive years (constant QALY model). When compared with the standard discount rate used in business $[1/(1+r)]^{j-1}$ this procedure provides similar values.
Each group of current median age A has a life expectancy x_A and a yearly variable U_j utility. Summing over all the discounted remaining years of life (1 to x_A) will provide the adjusted life years lost due to COVID-19. Thus, U_j is the utility ratio for each year in the rank $|A, A + x|$; r is a constant discount rate of 3.5%, selected according to the income of Spain (Attema et

al., 2012; Haacker et al., n.d.). Sensitivity analyses have been done for r = 3% and 4%. Some of the U_j values, not found in the references, have been computed by linear extrapolation of neighboring values. Table 1 summarizes the five-year values of the life table used, although we have computed and used year-by-year values from 50 to 95 years of age, extrapolating missing data.

Table 1. Summary by five-year values of the life table used for the calculation of quality-adjusted life-years (QALYs).

	Men			Women		
Age	Life Expectancy (LE)	U	LE Good Health	Life Expectancy (LE)	U	LE Good Health
0	80.48	0.793623	63.87	85.9	0.79350	68.13
50	31.85	0.687555	21.90	36.8	0.60030	22.10
55	27.42	0.674419	18.49	32.2	0.56993	18.32
60	23.20	0.599138	13.90	27.6	0.53354	14.71
65	19.21	0.589744	11.33	23.1	0.48085	11.10
70	15.43	0.556034	8.58	18.7	0.47353	8.85
75	11.91	0.522736	6.23	14.5	0.46622	6.75
80	8.80	0.489438	4.31	10.6	0.37504	3.99
85	6.25	0.456140	2.85	7.40	0.28387	2.11
90	4.39	0.383721	1.68	5.00	0.11491	0.58

Source: Authors' computation based on data from Spanish National Institute of Statistics [9] and Eurostat [10]. Data corresponding to 2017. Data of years not included in tables have been calculated by linear extrapolation of the nearest values.

The table highlights the so-called male-female mortality paradox: Females live longer but in a worse state of health [11].

To calculate the QALYs lost due to the pandemic in Spain, not only the total number of deaths has been considered, but also, for those patients discharged from hospital alive, a weight of morbidity considering their future QALYs (as expected by age and gender) to be reduced an average of 10% (Qw = 0.9Q0) forward discharges and 20% (Qw = 0.8Q0) for ICU discharges, following weights of a Markov model used for other chronic diseases [12– 14].

Additional data such as population statistics, figures related to influenza, and other values or ratios used in the text, have been obtained from the corresponding published institutional statistics [15–18].

3. Results

3.1. Magnitude of the Healthcare Problem: COVID-19 Outbreak versus Influenza

As of 27 October 2020, the estimated prevalence of COVID-19 in Spain was not very different from that of AH1N1 influenza, although it must be noted that there was an active outbreak of the former with about 20,000 new daily notifications at that time (accumulated incidence of about 500 per 100,000 habitants in 14 days) [16–23]. Table 2 comparatively presents the information together with Case Fatality Ratio (CFR) and Infectious Fatality Ratio (IFR) estimations up to that moment.

Table 2. Comparison of COVID-19 and A-Influenza data in Spain as of 27 October 2020.

Population	47,431,688 [1]			
	COVID-19	×100,000‡	Influenza	×100,000‡
Prevalence [2]	7,010,340	14,780	6,521,798	13,750
Confirmed [3]	1,116,738	2354	619,000	1305
Hospitalized	170,789	360	27,657	58
ICU	15,278	32	1800	4
Fatalities	59,422		3900	
Mortality (over [1])	0.13%	125.3	0.01%	8.2
CFR (over [3])	5.32%		0.63%	
IFR (over [2])	0.85%		0.06%	

Source: Authors' computation with data from sources [20–23]. ICU, intensive care unit. ‡ Inhabitants.

As evidenced by the figures, the prevalence in both cases was about 15%, but COVID19 is causing about six times more hospitalizations, over eight times more admissions in ICU, and fifteen times more fatalities. To facilitate comparison of these data with those in influenza reports, the alternative method suggested for reporting CFR in ongoing outbreaks has not been followed [24].

These data for COVID-19 incidence and prevalence in Spain as of that date were not very different from those in the UK, with about 20,000 new cases per day and over one million reported cases, as of 31 October [25]. The data correspond to moments of ongoing pandemic waves.

Table 3 provides the comparative figures between 27 October and 17 February, and includes the ratios used in our model based on the number of fatalities (n_f).

Table 3. COVID-19 data as of 17 February 2021 compared to data from 27 October 2020.

	27 October 2020	17 February 2021	Template
Prevalence [2]	7,010,340	9,814,476	Based on Pub.
Confirmed [3]	1,116,738	3,107,172	Reported
Hospitalized	170,789	306,727	3.45 n_f
ICU	15,278	26,477	0.3036 n_f
Fatalities (number)	59,422	84,150	n_f
Mortality (over [1])	0.13%	0.18%	
CFR (over [3])	5.32%	2.7%	
IFR (over [2])	0.85%	0.86%	

Source: Authors' computation with data from sources [19–26]. Population 47,431,688 inhabitants.

3.2. COVID-19 Related Expenditures

The «Framework for Estimating Health Spending in Response to COVID-19» report [27]—which includes 214 countries and territories, projecting volumes of people and costs between 8 March 2020, and 7 March 2021 (52 weeks)—has been published by the International Monetary Fund and models different scenarios, social distancing, lockdowns, and other variables. According to its conclusions, «effective social distancing and quarantine reduce the additional health spending from a range of US$0.6–1 trillion globally to US$ 130–231 billion, and the fatality rate from 1.2 to 0.2 percent, on average» (p. 2). As per this source, with satisfactory containment of the disease, increase in health expenditures due to COVID-19 would represent about 0.2–0.3% of the world's Gross Domestic Product (GDP) for 2019, «and fatality rate would be 0.1% of the population, on average, across countries» (p. 8).

The published costs that the disease is generating for healthcare systems, even when focused only on inpatient and outpatient care, are very variable, representing different health care approaches. Most of the reports are from the USA, where the healthcare provider is covered by a combination of payments by companies and users. In the most complicated cases, hospitalization due to COVID-19 rose to US$75,000 or even more. An average from US$9764 (for less severe cases) to about US$14,500 per person has been reported by the Kaiser foundation and other sources [28–31]. According to Avalere, COVID-19 hospitalizations could cost the U.S. healthcare system between US$9.6 billion and $ 16.9 billion in 2020 [32]. This represents between US$30 and US$50 per inhabitant. Reports from other countries with lower GDP, such as Mexico or Chile, show lower costs. There are also systematic reviews on the average length of stay for COVID-19 hospitalizations, which may be used for cost estimation [33].

Considering the available information and the reported costs for the Spanish Health Care System [34–38], the direct costs (to 17 February 2020) have been estimated and summarized in Table 4. Again, this information may not be exhaustive. The expenditure figure for asymptomatic cases is an estimate that includes over-the-counter medicines. It is not clear whether all hospitalizations in private centres have been included in these statistics but considering

that most cases are financed by the public system, this uncertainty has not been very significant.

Table 4. Estimation of direct healthcare costs for COVID-19 in Spain as of 17 February 2021 (direct cost including medication).

HC Provision	Number of Cases	Cost per Unit	After Discharge	Total
50% of cases with few symptoms	4,935,398	20 €		98,707,960 €
PC and OP health assistance	2,639,250	190 €		501,457,500 €
Hospital ward standard	246,236	3700 €	200 €	911,073,200 €
Hospital ward w/comp.	18,534	10,000 €	300 €	185,340,000 €
ICU (including ARDS)	25,548	27,000 €	350 €	689,796,000 €
Total				2,386,374,660 €
Per inhabitant				50 €
Per% of GDP				0.21%

Source: Authors' computation based on References [26,34–38]. OP, outpatient. PC, primary care. ARDS, acute respiratory distress syndrome.

According to our estimations, an average (cases in ward plus cases in ICU, excluding outpatient assistance) hospitalization costs about €5900 (US$7139). For Spain (2019), with a population of 47.3 million and a GDP of €1119,976M, COVID-19 health care (up to 17 February 2021) will represent about €50 per inhabitant, or around 0.21% of GDP, similar to the projection for all 2020 already commented on (0.2–0.3%) [27,30]. It must be taken into consideration that the disease is spreading rapidly, and this value only includes direct costs. The average, per day hospitalization cost was estimated at €369 (250–750), for an average length of stay of 15.9 days, obtained from a large series in France [33,39].

The pandemic has brought with it many other economic issues. Some of these are summarized in Table 5, in addition to the direct health care costs mentioned above (points 1–6).

Table 5. Summary of some relevant costs related to COVID-19.

	Cost Directly Linked to Health Care
1.	Primary care patients with minor symptoms.
2.	Primary care for patients later requiring hospitalization or during follow-up after discharge from hospital.
3.	Emergency assistance.
4.	Hospitalization and rehospitalization on ward.
5.	Use of mechanical ventilation devices.
6.	Intensive Care hospitalization and rehospitalization.
7.	Special treatments (monoclonal antibodies, convalescent plasma, etc.)
8.	Cost related to shrouding, storage, transfer, cremation or burial, and terminal cleaning of the rooms of the deceased.
9.	Operational costs, including staffing related to the increase of activity.
10.	Acquisition, training, consumption, and elimination of personal protective equipment for staff, including orderlies, maintenance personnel, security, cleaning, etc.
11.	Cost of the opportunity of delayed assistance to other diseases due to COVID-19.
12.	Outpatient drug costs, including pharmacy consultations and over-the-counter treatments.
13.	Transport (e.g., ambulances)
14.	Prescribed and over-the-counter medication.

	General population and business
1.	Protective measures, including panels, gloves, hydroalcoholic gels.
2.	Related to home lockdown for adults and children, including babysitting for workers with children remaining locked down at home.
3.	Related to labor reduction, readaptation, or loss.
	Governmental
1.	Reorganization and adaptation of public services, including police, port, and airport controls, quarantine compliance controls, military emergency services, their protective equipment, and cleaning agent's consumption.
2.	Relief plans, extra services, and supports for vulnerable people (unemployed, elderly, etc.)

3.3. Cost-Effectiveness of Vaccination

According to data reported as of 17 February 2021 [26], we have estimated that 554,539 QALYs (539,367–577,679) have been lost either directly due to mortality from COVID-19, or as a result of future morbidity, without taking into account additional losses, such as the opportunity costs of delayed treatments for other diseases as a result of the pandemic and other hidden costs [40]. Table 6 depicts a template for calculating the QALYSs referred to as the total number of fatalities, a data usually consistent in demographic statistics.

Table 6. Template for calculating COVID-19 adjusted and discounted years (QALYs) resulting from direct mortality and expected morbidity, based on the total number of fatalities (n_f).

n_t = Total Number of Fatalities	Number	Average Age	Life Expectancy	L/Free of Disease	QALY (Q_0)		$Qw = 0.2Q_0$	Total Q
Men alive after ICU	$0.10242n_t$	62.6	21.2	12.8	8.6	(8.2–9.0)	1.7	N^*Q_w
Women alive after ICU	$0.11466n_t$	62.9	22.3	12.7	7.3	(7–7.6)	1.5	N^*Q_w
							$Qw = 0.1Q_0$	
Men alive after ward hospitalization	$1.25436n_t$	66.5	18.3	10.6	7.4	(7.1–7.7)	0.7	N^*Q_w
Women alive after ward hospitalization	$1.40431n_t$	68.1	17.8	9.7	6.0	(5.8–6.3)	0.6	N^*Q_w
Subtotal (morbidity)	Σ							
Men death by age (hospital and home)							$Qw = Q_0$	
<65	$0.03702n_t$	52	30.1	20.2	11.3	(11.2–11.4)	11.3	N^*Q_w
65–74	$0.06664n_t$	70	15.5	8.6	6.3	(6.3–6.4)	6.3	N^*Q_w
>74	$0.42459n_t$	80	12.3	6.4	3.7	(3.6–3.9)	3.7	N^*Q_w
Women death by age (hospital and home)							$Qw = Q_0$	
<65	$0.03306n_t$	55.0	27.1	17.5	9.8	(9.7–9.9)	9.8	N^*Q_w
65–74	$0.05951n_t$	70.0	15.5	8.6	5.6	(5.5–5.8)	5.6	N^*Q_w
>74	$0.37918n_t$	80.0	12.3	6.4	3.7	(3.6–3.9)	3.7	N^*Q_w
Subtotal (mortality)	Σ							

Source: Authors' computation with data from sources [12,13,26,41–43]. Discount rate (3%, 3.5%, 4%).

The question of age and morbi-mortality for COVID-19 will give rise to issues, such as whether the patients that have died with the disease represent a subset of ill persons with less QALY than the average for the age, or for which population it would be more cost-effective to program early vaccinations [44]. At an estimated cost of €30 per shot (vaccine plus transport, storing, and administration) [45,46], the following table (Table 7) offers the cost-effectiveness analysis for different percentages of vaccine efficacy and discount rates (r = 3%, 3.5%, 4%), and different percentages of the population included in a vaccine program of two shots.

Table 7. Incremental cost-effectiveness ratio (ICER) for COVID-19 vaccine adjusted by different percentages of efficacy and population vaccinated in Spain with data as of 17 February 2021.

100% Population	%Vaccine Efficacy▶	50	60	70	80	90
Overall QALY ($r = 3\%$)	539,367	10,553	8794	7538	6595	5863
Overall QALY ($r = 3.5\%$)	554,539	10,264	8553	7331	6415	5702
Overall QALY ($r = 4\%$)	577,679	9853	8211	7038	6158	5474
80% Population	**%Vaccine Efficacy▶**	**50**	**60**	**70**	**80**	**90**
Overall QALY ($r = 3\%$)	539,367	8442	7035	6030	5276	4690
Overall QALY ($r = 3.5\%$)	554,539	8211	6843	5865	5132	4562
Overall QALY ($r = 4\%$)	577,679	7882	6569	5630	4926	4379
70% Population	**%Vaccine Efficacy▶**	**50**	**60**	**70**	**80**	**90**
Overall QALY ($r = 3\%$)	539,367	7387	6156	5276	4617	4104
Overall QALY ($r = 3.5\%$)	554,539	7185	5987	5132	4491	3992
Overall QALY ($r = 4\%$)	577,679	6897	5748	4926	4311	3832

Source. Authors' calculation. Cost per two shots, vaccine plus inoculation (30 € each).

The incremental cost-effectiveness ratio (ICER) was calculated by dividing the incremental cost resulting from vaccination by the measure of health outcome (incremental effect in QALYs) to provide a ratio of 'extra cost per extra unit of health effect' [47]. ICERs may be compared across disease areas and are evaluated with a predetermined cost-effectiveness threshold.

Vaccination of about 70% of the Spanish population, with a conservative 70% ratio of efficacy and two shots, will result in €5132 (4926–5276) per QALY gained.

For comparison, the cost-effectiveness threshold, or basal-case ICER, was set between €22–33,000. NICE (National Institute for Health and Care Excellence) aims to spend less than £25,000 (€27,500) per QALY. A similar value (CAN$40,000 = €27,200) was set for other vaccination program by Brisson et al. [48].

It must be considered that the ICER threshold depends on a willingness to pay, and in consequence, on GDP. The World Health Organization suggests referring cost-effectiveness to GDP [49]. Although US$50,000 has been considered for a long time in the USA as the limit for the cost-effective threshold, this value has been criticized as being low [50]. The US threshold (2017 data) for very cost-effective (considered as less than one times GDP) has been reported to be < US$59,532; for cost-effective (between 1–3 times GDP) <= US$178,596; and considered not to be cost-effective (greater than three times GDP) when > US$178,596 [51]. Neumann et al. [50] suggest as a rule US$50, 100, and 200 thousand, for each range, matching very roughly with less than one times GDP per capita, between one- and three-times GDP, and over three times GDP. In any case, the prediction of our model for COVID-19 vaccine cost-effectiveness is well under the threshold; the vaccine is highly cost-effective [52,53]. Table 8 overviews the ICER of some vaccination reports in the last two decades:

Table 8. Incremental cost-effectiveness ratio (ICER) of some vaccination plans reported in the literature for the last two decades with conversion to EUR at the corresponding date for the year.

Vaccination	Target Population	ICER	Currency	Rate (1€→)	ICER (€)	d/Rate	Article	Year	First Author
Pneumoco	Adults 65 and over	11–33,000	€		11–33,000	0–5%	Bibliometric	2000	Ament
Lyme disease	Resident endemic areas	62,300	$US	(2001 = 0.89)	70,000	3%	Modeling	2001	Shadick
Influenza	Adults 50–64 y/o	10,766	£	(2005 = 0.67)	16,069	NA	Modeling	2005	Turner
Influenza	Children 6m–4 y/o	<25,000	$US	(2006 = 1.25)	≤19,925	NA	Modeling	2006	Prosser
H Papilloma (HPV)	12–24 y/o females	3000	$US	(2007 = 1.37)	2190	3%	Modeling	2007	Insinga
Papilloma (HPV)	12–24 y/o females+ males	16,000	$US	(2007 = 1.37)	11,679	3%	Modeling	2007	Insinga
H Papilloma (HPV)	12 y/o females	21–31,000	$CAN	(2007 = 1.46)	30,666–45,260	3%	Modeling	2007	Brison
A Hepatitis	Travellers	26,046	$US	(2008 = 1.46)	17,840	5%	Bibliometric	2008	Anonychuk
A Hepatitis	Health care workers	129,046	$US	(2008 =1.46)	88,388	NA	Bibliometric	2008	Anonychuk
A Hepatitis	Military	16,332	$US	(2008 = 1.46)	11,186	NA	Bibliometric	2008	Anonychuk
A + B Hepatitis	Children	<35,000	$US	(2008 =1.46)	<23,972	NA	Bibliometric	2008	Anonychuk
H Papilloma (HPV)	NA	32,884	€		32,884	NA	Modeling	2008	Bergeron
Herpres Zoster	Adults 60 and over	20,400	£	(2009 = 0.89)	22,921	6%	Modeling	2009	Van Hoek
pH1N1 Influenza	6m–64 y/o	8000–52,000	$US	(2009 = 1.39)	5755–37,410	3%	Modeling	2009	Prosser
Rotavirus	Children < 5 y/o	23,298	£	(2009 = 0.89)	26,178	3.5%	Modeling	2009	Martin
Rotavirus	Children < 5 y/o	61,000	£	(2009 = 0.89)	68,539	3.5–3%	Modeling	2009	Jit
H1N1v Influenza	Age groups	2733–3215	£	(2010 = 0.86)	2733–3215	3.5%	Modeling	2010	Baguelin
H Papilloma (HPV)	12 y/o females	1917	€		1917	3%	Modeling	2010	Olsen
H Papilloma (HPV)	Girls 12 y/o	3583	€		3583	3–5%	Modeling	2015	Olsen
Influenza (IIV3)	Adults 65 and over	3690	$US	(2016 = 1.11)	3324	3%	Modeling	2016	Raviotta
Influenza (TIV)	Adults 65 and over	10,750	€		10,750	0%	Modeling	2018	Capri

Source: Authors' compilation.

The numerator of the cost/quality ratio (i.e., the cost of vaccination in Spain) is not expected to increase, as the cost per dose may even be reduced by competition between vaccines, and the Spanish population will not experience appreciable changes in the short term. However, the denominator (years lost) continues to grow with a significant number of new deaths each day, so the ICER will progressively decrease as the pandemic continues to spread.

In other words, for every day of active illness, there will be a reduction in the ICER, as this represents a continuous increase in the loss of QALYs (denominator). However, if the number of patients alive after contracting COVID-19 (and consequently having immunity, assuming this lasts a reasonable time) increases substantially, it would also impact on reducing the cost-effectiveness of the vaccine.

In addition, vaccination will generate savings in health expenses and alleviate the economic consequences of the pandemic in both the health insurance sector and private hospital centres, which, as a result of COVID-19, are currently suffering wage cuts, layoffs, and risk of financial unfeasibility [54]. This is just one of the economic issues related to COVID-19.

4. Discussion

In situations of uncertainty, when reliable data are either not available or arrive late, or the pressure on care is so great that statistics cannot be relied upon, the use of simple mathematical estimation models can provide information reliable enough for health planning, since in this case a highly accurate numerical assessment is not required, but rather a range. The consideration of COVID-19 as a serious issue must be easily deduced, not only from the data in tables above, but also from the social and political movements and urgent plans for action issued by national and international authorities, EU included [55]. The data in this paper refer to a disease with morbidity and mortality in progression, but what is important is that the model allows easy recalculation with the updating of information.

The procedure followed, including how CFR and IFR were computed, may have some limitations: Firstly, the method may estimate data that could not be fully accurate. Secondly, it is better to compute CFR during an active outbreak by the ratio death/(death + recovered) [56]. However, they have been considered as one-day 'snapshots' analyses and carried out, in the case of October values, homogeneously with data related to influence for easy comparisons. The importance and impact of our approach are further emphasized by the constant interest in the costs of the pandemic by the media [57], with estimations of values not far from our own results. Although, considering a relatively wide range for imprecision, the values serve as a proxy for the severity of the pandemic as compared to influenza and the economic benefits of vaccination.

A further constraint comes from the fact that economic evaluations of infectious disease interventions are often based on predictions from systems of ordinary differential equations (ODEs) or Markov models, either static or, more typically, dynamic ones that consider herd immunity, which is crucial to avoid overestimation of infection prevalence [58–60], although other approaches are possible [61]. Our simplified model may be criticized for not following that trend. However, studies of herd immunity on COVID-19 are already available [62], with seroprevalence rates very low (about 5%). There is also the issue of changing age, as the dynamic model could predict an increase in the average age at infection after immunization, which could impact the estimate of the cost-effectiveness of the program, particularly in this case of serious disease as a function of age. According to our model, about 80% of fatalities already correspond to subjects aged over 74. A multinational meta-analysis, with a total of 611,583 subjects, showed that 82.9% of the fatalities were for those 70 and over, very close to our model considering the four years (70–74) range difference and regional variations [63]. The fourth series of mortality data from MoMo [5] do not show significant changes in mortality ratios among waves by age, but it is true that the vaccination effect is not included, as the number of cases vaccinated up to 17 February that could be included in the mortality figure is to be considered nearly zero. Additionally, this limitation may result in less relevant, considering that constant models tend to underestimate the cost-effectiveness of the immunization program [59]. This paper presents a simplified mathematical model to establish a range for the cost-effectiveness of COVID-19 vaccination, rather than the procurement of a totally accurate computation, which in any case does not seem essential as long as the values obtained are well below the cost-effectiveness threshold.

If SARS-CoV-2 behaves as A(H1N1) influenza with periodic outbreaks—something not improbable as both are RNA viruses—even with measures of social distancing and periodic lockdowns (each time less popular among citizens), Spain should expect, in the next 10 years, between 7 and 12 million of confirmed cases, and over 400,000 deaths (at decreasing ratio of about 45,000 per year), a value consistent with estimations in the UK by Sandmann et al.

[64]. Following this reference—assuming 75% efficacy, 10 years protection and 10% of re-vaccination, discount rate of 3.5% and monetized health impact at £20,000 (€22,000)—vaccination (plus physical distancing) versus no vaccination will represent between €6.11 and €21.95 million economic gain or Net Monetary Benefit (NMB) per million population (i.e., €288.9–€1038.5 million for Spain in ten years) [64]. Values are consistent after sensitivity analyses and the proportion of mortality in the UK. Simulations studies advocate efficacies of at least 60% [65]. This brings up the issue of the unknown duration of immunoprotection. If a periodic COVID-19 vaccination schedule were to be established, i.e., a schedule similar to that for other viral processes, such as influenza, the cost-effectiveness of vaccination could change appreciably.

The method of cost-effectiveness has been chosen because among the main indicators used in the economic analysis of healthcare planning, (cost-benefit, cost-effectiveness, and cost-utility), the effectiveness perspective is useful for decision-making on how best to allocate resources, while the cost-benefit ratio analysis helps decision-making on overall resource allocation. Quality-adjusted life year analysis allows direct comparison of a wide range of health interventions [66,67]. For QALYs, the use of utility scores from a life table (Table 1) eases the calculation of the adjusted number of years lost for the average age in each of the groups studied. The median age of about 70 for patients admitted in Spanish hospitals for COVID-19 [21] is not far from data from another report, also from a country with a National Health System, reviewing 16,749 cases [68].

Additional reduction for chronicity, mainly resulting from permanent inflammatory handicaps (e.g., pulmonary fibrosis) requiring extra healthcare resources, has been considered in survivors in an average of 10% [$Q_w = 0.9\ Q_0$] in cases of ward discharges, and 20% [$Q_w = 0.8\ Q_0$] after ICU discharge. Similar utility scores have been obtained with Markov model methodology in cases of other chronic diseases (e.g., in Diabetes Mellitus, a disease that also requires periodic visits and controls) [69,70]. Sensitivity analyses of this utility score at ±10% (i.e., 0.09–0.11, and 0.18–0.22, respectively) maintain significant QALY gains in all cases; Q_w could be additionally adjusted for protection length of time and annual revaccination rate. A weighted variation related to age could also be considered.

Except for some promising drugs currently in development, there is no effective treatment for COVID-19. The first option considered was to examine the role that herd immunity might have. We have already predicted that herd immunity would not play a major role as a barrier to COVID-19 [4], as confirmed by subsequent serological studies [71]. Moreover, data suggest transmission, even from asymptomatic patients, in many cases [72].

With the results of over 365,000 tests done in England showing that antibody response to SAR-CoV-2 wanes over time [73], and reinfection cases reported [74], the possibility of herd immunity as a barrier remains low, although it must be admitted that the expected severity of reinfected cases should, at least theoretically, be lower, due to the residual memory effect of the immune system, which is characteristic of infections [75– 77]. Therefore, at present, there is only one rational, proactive measure to increase herd immunity and effectively reduce the number of cases of COVID-19, that being vaccination plans [78].

A cost of the vaccine of about £10 for the product, with another £10 for administration, as estimated by Sandmann et al. [64], which seems reasonable for a country with a National Health System. According to a governmental report in Spain, each dose for the vaccine of influenza costs the Spanish Health Care System an average of €4.3, and the shot about €6.0 [79].

Considering not only the cost of extra protection measures and time required for isolation of health professionals prior to COVID-19 vaccine administration, and the high demand for a new product, but also the massive acquisitions already announced—it must be remembered that the EU has made arrangement for buying 300 million doses of the Sanofi-GSK vaccine—

a range between 20–30 Euros for each shot (vaccine plus administration) when bought at great volume seems reasonable [45,80–82].

According to Reuters, there is a plan to inoculate about 50 million US citizens for about US$40 per person (€34.5) [83]. Other elements that could influence price are the low temperature condition for transport and storage, particularly in developing countries, where the role of interventions may differ [84–86]; the forecast of scenarios may change in each case [87]. It should be noted that our study refers to two doses of vaccine, but there is no evidence to indicate that COVID-19 will not require revaccination, even for life. A plan in this case, like that of influenza, will represent about 10 times the cost indicated [79].

Finally, there may also be factors not captured in the QALY formulas, including indirect costs, the value of returning to normal life, the effects on mental health (anxiety, depression, fears of losing jobs, and lockdown, production losses, etc., that will additionally increase the benefits of vaccination. In other words, that cost-effectiveness measured with the standard procedures may not be the only thing that matters [88,89].

5. Conclusions

Left alone, successive COVID-19 outbreaks could represent between 7 and 12 million confirmed cases and over 400,000 deaths in Spain in 10 years. Vaccination against SARSCoV-2 is the only reasonable approach and seems clearly indicated after analysis of the risks of getting vaccinated versus not getting vaccinated, together with the vaccine data available [1,2].

The cost estimates with our mathematical model are simple, easily reproducible, and fit well with other available data. Data of Table 6 may be used for other purposes, e.g., in case of shortage of vaccines, to compare different commercial products.

Data allows us to appraise an ICER of 5132 euros (4926–5276 euros)—even while using a conservative approach of vaccinating about 70% of the Spanish population with a vaccine efficacy of about 70% (two injections). This is a very cost-effective ratio as a result of a vaccination plan; furthermore, the ratio improves (i.e., the cost decreases) for each day of new cases reported after 17 February 2021.

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2.3.3. Comments to paper III.

Two moments were chosen for gathering information, 27 October 2020, and 17 February 2021. Although they were not good times in epidemiological terms, since there was an active outbreak of the disease, the dates had advantages from the point of view of information recording. In addition, for the comparison of the October information, there was data from the UK available at a very similar date. It is true that the UK has 1.4 times the population of Spain, but its National Health Service (NHS) has a long history, with many similarities to the Spanish health system, and the UK has extensive experience in health economics, as demonstrated by the early publication of the Imperial College on coronavirus from an organised team (Neil M et al., 2020).

With such an ongoing situation, the paper had the main intention of casting some light onto the darkness of the unknown situation by providing a simple model to estimate cost-effectiveness based on a robust data, the mortality figures. This information is obtainable from different sources such as the Statistics Institute, Social Security, Taxes database, etc. Once more, the value was not expected to be completely precise, something virtually impossible in current circumstances, but to shed a light on the expected range.

The analyses have only considered part of the costs. Not even the opportunity costs, resulting from delayed care for other diseases, have been included. The paper summarizes a list of costs (Table 5) that should be further considered in the future. Considering that the results are well below the threshold of about US$ 50,000 that, with some variations, depending on the wealth of the country, is typically considered as the limit for cost-effectiveness, the vaccination plans remain within a very attractive range, even accepting a percentage of uncertainty.

However, several uncertainties remain. It is not clear if annual vaccination will be required, which would noticeably change the figures provided in this paper. There is also the question of the different strains of the virus, their susceptibility to the developed vaccines or whether new vaccine developments will be needed, with their corresponding cost impact unknown for the time being.

On the other hand, it was a conservative first approach, with the ICER changing every day as it was taken from data during an active outbreak in Spain. Since it is not expected for the Spanish population to suffer significative changes in the short term, with a total estimated cost for two shots plus administration set at a price of €60 (€30 each), the ICER value should

improve over time. Only between the two dates (less than four months difference) the ICER has been reduced by about 40%. Again, there is no proof that the tendency will continue to follow this pattern.

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2.4 ADDITIONAL RESEARCH: Impact of COVID-19 on Workforce and Education

This subchapter includes further research, either presented to congresses or to eventually to be published at a later time and out of the requirements of the thesis by publication. It follows the same structure as above.

2.4.1. Concerns of frontline health workers after COVID-19: a bibliometric analysis on topics and fields.

Abstract

A statistically significant sample (n = 207) of the annual production of scientific nursing papers for the years 2019 and 2020 has been selected for a comparative bibliometric analysis, to detect changes in the variables topics and fields following the outbreak of the COVID-19 pandemic. Nonparametric methodology has been applied to determine the relationship between the two qualitative variables (topics and fields) in these two years, for 95% confidence level (d = 0.05), 85% confidence interval (CI), and (50%) of attribute and non-attribute (p = q = 0.5).

We have observed a significative change (X^2 = 15.32; p = 0.001559) in topics between 2019 and 2020. Articles focused on personal protection and barrier elements have increased from 2% to 7%; professional stress and related topics have increased from 16% to 27%; while a discrete reduction (from 63% to 51%) has been observed in the articles focused on management and organization.

When the trend is analysed by area, the statistical significance is lower (X^2 = 7.25; p = 0.02665), as the most relevant variation falls in the field of nursing homes, where the publications dealing with organisation and management aspects have doubled (from 8% to 16%).

In conclusion, this study shows that the main trend change (2019 v. 2020) of published nursing science articles, when referring to nursing homes, is the increased interest in organisational topics, while in the other nursing fields (mainly primary care), publications show an increase in topics related to personal protection and professional stress.

Bibliometric analysis provides useful information on the working environment and issues of concern to nurses — the frontline of the fight against COVID-19 — as well as its trend, as an alternative source to direct survey information, which places an additional burden on an already oversaturated staff.

Key words

Bibliometric analysis, COVID-19, SARS-CoV-2, coronavirus, working environment, care planning, burnout, nursing homes, pandemic, health planning, personal protective equipment.

Introduction

Health workers, and in particular nurses, who are the most numerous within this group and on the front line in the fight against the pandemic, have not been able to escape the extraordinary situation produced by the outbreak of COVID-19, the burden and psychological pressures of the job, and the bewildered and frustrated society of which they are a part.

Changes in the work climate can also be analysed through the literature. Bibliometric analyses based on series or historical data require grouping the multitude of data for classification

(Perkins, 2003, p. 229). In the case of applying such analysis to scientific literature, there is the advantage that the information is easier to obtain, thanks to powerful search engines for academic publications. In addition, the health sciences have implemented mathematics in their studies, mainly statistics (DeShea & Toothaker, 2015; Devore & Berk, 2012; Gordon, 2012; Scammell, 2010) In the bibliometric approach, these techniques can become sophisticated, including piecewise regression (Bornmann & Mutz, 2015), keyword extraction algorithms and alternative algorithms (altmetrics) usable not only as an index of impact metrics of papers but applicable to other settings (Zahedi et al., 2014).

Nurses play a key role in the healthcare system's response to the COVID-19 challenge, as they not only provide direct care to patients, but are an essential element in their training and education, which is essential to reduce the risk of exposure to infection. Their tasks require, in addition to adequate staffing, professional team planning that includes measures to assess the work climate and minimise physical and emotional impact, and a systematic response to stress factors (Fernandez et al., 2020).

There is ongoing work in this area, such as a project in the Philippines, which included 325 nurses, including 123 (38.8%) cases with dysfunctional levels of anxiety. The results were encouraging and open the door to the idea that it is not only possible to measure the degree of dysfunctionality caused by the pandemic, but also to develop measures to minimise the impact on nurses (Labrague & De los Santos, 2020). Based on these results it is possible to promote actions for the clarification of the organisational purpose and identify steps to address problems and challenges; a detailed explanation of the actions, showing empathy on the part of management or supervisory positions, emotional support and the implementation of adequate protection and training measures, and a better knowledge of the material and procedures, the shortcomings of which have been detected in the study (Hofmeyer & Taylor, 2020).

Material and Methods

This study compares selected aspects of nursing publications between 2019 and 2020. Some 4,000 published papers have been reviewed, of which 414 were finally selected (details are presented in an appendix) to enable an inferential analysis of the total number of publications in period.

The search procedure and selection of publications was based on the SJR (Scimago Journal & Country Rank) database, which establishes an independent indicator, after analysing the weighting of citations and the centrality of the vector (eigenvector) of the graph, allowing the importance of a node in the network to be determined. It is designed for use with complex and heterogeneous citation networks such as Scopus, and includes 30,891 scientific journals, which offers advantages over other search procedures.

The search and selection of publications in the subject area 'nursing' through SJR yielded 643 journals. The universe size, or total number of articles published (*N*), was first estimated, assuming 12 issues per year (i.e., one issue per month, which gives an additional safety margin, as not all journals are published monthly), and an average of 20 articles per issue, resulting in an estimated total number of articles (*N*) of 643 • 12 • 20 = 154,320 publications. Applying the indicated precision and confidence criteria, $Z_{\alpha/2} = 1.44$ (which corresponds to the CI 85%), $p = q = 0.5$ and $d = 0.05$, for $N = 154{,}320$, the result is $n = 207$, with the well-established formula (Devore & Berk, 2012):

$$n = \frac{NZ_{\alpha/2}^2 pq}{[d|2(N-1)] + \left[Z_{\frac{\alpha}{2}}^2 pq\right]}$$

The following criteria were used for the selection of the articles:

1) The article must contain sufficient information, preferably through access to the full text of the publication.

2) It must include the Digital Object Identifier (DOI), so that a subsequent quality control check can be carried out, and the article could be revisited quickly if necessary.

3) It should not refer to aspects of specific specialities or nursing units (cardiology, intensive care, nephrology, oncology, etc.).

4) It should focus on the nursing staff, their protection, organisation, or procedures, and not on aspects related to techniques or patient care, unless they are a consequence of changes or adaptations to the circumstances of COVID-19.

To reach the required sample (207 valid articles) with these criteria, it was necessary to expand the search, using the following databases: Wiley Online Library,[4] Worldwide Science,[5] EBSCOhost Research Database,[6] Microsoft Academic[7] and Google Scholar,[8] using the Boolean condition (nurse or nurses or nursing) AND (COVID-19 or coronavirus), for the sample relating to 2020 publications and removing the AND condition for 2019 data.

The first information dump contained duplicate publications, and this was checked by computerised sorting by criteria A-Z of the Digital Object Identifier (DOI) field in a spreadsheet. The duplicate references detected in this way were eliminated and replaced after a new search, until the required total of 207 publications without repetition was reached for each of the two years (2019 and 2020).

This exhaustive filtering was carried out so that the articles analysed in detail were representative of the problems that COVID-19 has conditioned in nursing staff and, therefore, it was necessary for this issue to be the central element of the publication. As indicated, publications with a specific focus on techniques of nursing specialities were excluded.

The 414 publications finally selected were analysed by topics and fields. The topics (first variable of the analysis) was grouped as follows:

1/ relating to personal protection and its elements.

2/ relating to the psychological domain, fears of contagion, burnout, etc.,

3/ relating to clinical care practice itself (techniques, clinical methods if directly related to, or modified due to, COVID-19) .

4/ relating to aspects of management, organisation, education, public health, etc.

As for fields (the second variable in the analysis), they have been classified as:

A/ general nursing, primary care or not specified in the publication.

B/ hospital nursing.

C/ residential centres, nursing homes or similar.

After obtaining the data, the analysis of the variations between the publications corresponding to the year immediately prior to the appearance of COVID-19 (2019) and the year 2020 was carried out using non-parametric statistics.

Results

Data related to publications for years 2020 and 2019 is presented in Tables 1 & 2**.**

[4] *https://onlinelibrary.wiley.com/ (accessed on 15 December 2020).*
[5] *https://worldwidescience.org/wws/desktop/en/results.html (accessed on 15 December 2020).*
[6] *https://www.ebsco.com/ (accessed on 18 December 2020).*
[7] *https://academic.microsoft.com/home (accessed on 18 December 2020).*
[8] *https://scholar.google.es/schhp?hl=es (accessed on 20 December 2020).*

Table 1
Summary of topics and fields in 2020 publications.

Topics ►	Protection (1)	Psy/Mental H. (2)	Proceed. (3)	Management (4)	
▼ Fields	n_1 (%)	n_2 (%)	n_3 (%)	n_4 (%)	
General (A)	12 (8)	50 (34)	15 (10)	71 (48)	148
Hospitals (B)	2 (8)	6(24)	8 (32)	9 (36)	25
N. Homes (C)	1(3)	0 (0)	7 (21)	26 (76)	34
	15 (7)	56 (27)	30 (15)	106 (51)	207

Note. Authors' work.

Table 2
Summary of topics and fields in 2019 publications

Topics ►	Protection (1)	Psy/Mental H. (2)	Proceed. (3)	Management (4)	
▼ Fields	n_1 (%)	n_2 (%)	n_3 (%)	n_4 (%)	
General (A)	3 (2)	22 (15)	23 (16)	108 (73)	156
Hospitals (B)	1 (4)	10 (40)	9 (36)	14 (56)	34
N. Homes (C)	0 (0)	2 (6)	6 (18)	9 (26)	17
	4 (2)	34 (16)	38 (18)	131 (63)	207

Note. Authors' work.

The data show an increase in publications on protection issues from 4 (2%) to 15 (7%), as well as mental health and related topics from 34 (16%) to 56 (27%), with a reduction from 131 to 106 (63% to 51%) in management, and a less appreciable change in proceedings. These differences are statistically significant (X^2 = 15.32; p = 0.001559) (Table 3).

Table 3
Differences in topics between the two years (2019 -2020) n(%)

Year▼ /Topics ►	Protection (1)	Psy/Mental H. (2)	Proceed. (3)	Management (4)	
2020	15 (7)	56 (27)	30 (14)	106 (51)	207
2019	4 (2)	34 (16)	38 (18)	131 (63)	207
X^2= 15.32 p= 0.001559	19	90	68	237	414

Note. Authors' work.

The number of articles related to organisation or management has decreased from 131 (63%) to 106 (51%), but when analysing the data broken down by field, the number of articles referring to the organisation of nursing homes has increased, as can be seen in Table 4, which shows a 100% increase in the number of publications related to nursing homes:

Table 4
Differences in fields between the two years (2019 -2020) n(%)

Year ▼ /Fields ►	A-General (%)	B-Hospital (%)	C-Nursing homes	
2020	148 (72)	25 (12)	34 (16)	207
2019	156 (76)	34 (16)	17 (8)	207
X^2 = 7.25 p= 0.02665	304	59	51	414

Note. Authors' work.

This lower significance of the X^2 value is related to the fact that practically all the weight falls on this difference between the publications referring to nursing homes, whose percentage, as mentioned above, has doubled (from 8% to 16%), while in the other fields the percentage variations are much less relevant. The grouping of the data in a 2 x 2 table (not shown) with the application of the Yates adjustment only serves to highlight what has already been obtained by the previous statistic.

Discussion

According to a report published by the World Health Organization (WHO), in collaboration with the International Council of Nurses (ICN) and the Nursing Now campaign, there are an estimated 28 million nurses and midwives worldwide. Despite some increase in recent years (Figure 1), there is still an estimated shortfall of nearly six million, and the WHO and its partners have issued an urgent call for investment in nursing and midwifery workforce. (World Health Organization, 2020).

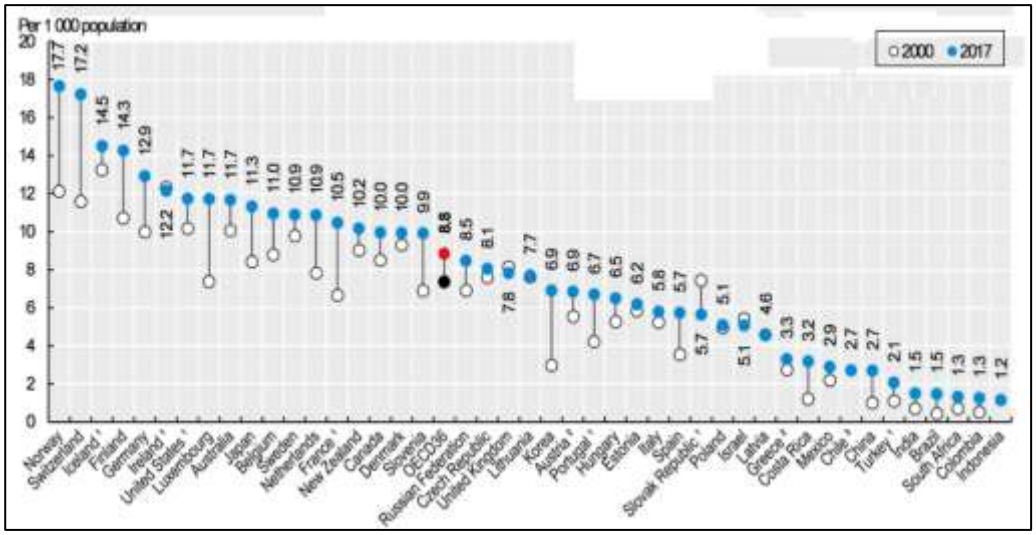

Figure 1. Practising nurses per 1,000 population for years 2000 and 2017. Austria and Greece report only nurses employed in hospitals. Data in Chile refers to all licensed nurses. Source the Organisation for Economic Co-operation and Development (OECD) Health Statistics 2019. *StatLink* http://doi.org/10.1787/888934017386

It should be noted that the data in the figure above, provided by the OECD, also includes nurses working in the health sector as managers, educators, researchers, etc.

Just when awareness of the nursing and midwifery shortage was expected to increase with the declaration of 2020 as the International Year of Nurses and Midwives, commemorating the 200th anniversary of the birth of Florence Nightingale (National League for Nursing, 2020), the COVID-19 pandemic broke out, creating work overload, psychological pressure and occupational risks of contagion, illness and death rarely seen in the recent history of nurses and midwives.

Beyond the public health sphere, the consequences of the pandemic extend to economic, occupational, and educational activity, family life, leisure, and social events, forcing the adoption of protective and distancing measures not previously used in general and the implementation and analysis of different quarantine models and options (Mishra et al., 2020).

This situation also affects nurses, as an integral part of society. They need to spend considerable time on protective measures and cope with increased activity, which has pushed teams to the limit. Issues such as post-traumatic stress, anxiety, depression, transitioning through emotional changes, including fear of the risk of transmitting the disease to family members, among other resilience-related issues, are everyday factors in this workforce, as paradigm of

a society whose patterns have notably changed (Luceño-Moreno et al., 2020). Bibliometric studies make it possible to analyse these aspects without overburdening staff with surveys or other evaluation procedures.

In summary, this work has one main objective, to obtain information on the concerns of nursing as reflected in scientific publications related to COVID-19, and two subordinate objectives; the first of these is its disaggregated analysis by subject and field, and the second, the comparison between the publications of 2020 related to COVID-19 and the publications of the year immediately prior to its appearance, to assess how the profile of the work published by nursing has changed after the appearance of the SARS-CoV-2 virus.

Our data show that there is a significant increase in publications related to barrier or protective measures, fatigue, psychological stress, and resilience in general, mainly in primary care setting, while in nursing homes, where staffing is even tighter, and where their lockdown has sometimes been necessary, publications related to reorganisation of the facility have been more common. These data add further information together with the hope that, through organisational changes, family and social support and empathy on the part of supervisors and managers, the working environment of frontline nurses, to whom this article is mainly dedicated, can be improved (Hofmeyer & Taylor, 2020; Labrague & De los Santos, 2020).

Conclusions

This paper shows, through bibliometric analysis of scientific publications from the years 2019 and 2020, that the COVID-19 pandemic has generated notable changes in nursing staff, increasing questions and requirements about protective measures, generating a notable increase in psychological alterations, including stress, burnout and related, and revealing a need for reorganisation of nursing home management. In addition to highlighting these aspects, this paper also provides a semi-quantitative assessment of each of these issues.

In the light of the data from this study, the following lines of future work are proposed:

1/ The review of protection protocols, knowledge of and compliance with barrier measures, as well as the analysis of whether adequate protection elements that technically should be in place are available. This point is particularly important in view of the significant number of deaths of healthcare workers due to COVID-19.

2/ In-depth analysis and action plans to mitigate professional stress, burnout and other elements of the psychological area (Guixia & Hui, 2020) working to improve aspects of resilience to the pandemic.

3/ Review of the organisation and work plans in home care centres, redesigning them if necessary, so that, while maintaining their economic viability, given that with some exceptions they are not publicly owned, they can continue to house our elderly with guarantees for both residents and carers.

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ANNEX: Details of articles reviewed by DOI, topics and fields.

Year 2019

#	DOI: https://doi.org/	Topics (1-4)	Fields (A-C)	#	DOI: https://doi.org/	Topics (1-4)	Fields (A-C)
1	10.1111/ijn.12803	4	A	66	10.1111/iwj.13021	3	C
2	10.1111/scs.12669	4	A	67	10.1111/jonm.12898	4	A
3	10.1111/ijn.12777	4	A	68	10.1002/nur.21984	3	A
4	10.1111/wvn.12401	3	B	69	10.1111/jan.14023	2	A
5	10.1111/jonm.12764	4	B	70	10.1111/nuf.12370	4	A
6	10.1111/jnu.12510	4	A	71	10.1111/jocn.14889	4	C
7	10.1111/jonm.12757	4	A	72	10.1111/phn.12699	3	A
8	10.1111/nuf.12394	4	A	73	10.1111/jocn.15091	4	A
9	10.1111/jgs.16051	2	C	74	10.1111/cod.13301	1	A
10	10.1002/nop2.316	3	B	75	10.1111/inr.12542	4	A
11	10.1002/nur.22003	4	B	76	10.1111/jocn.14961	4	A
12	10.1111/nhs.12601	4	C	77	10.1111/jan.13962	4	C
13	10.1002/nop2.414	4	B	78	10.1111/scs.12796	3	A
14	10.1111/nup.12270	4	A	79	10.1111/ajag.12637	2	A
15	10.1111/jonm.12817	4	B	80	10.1111/jonm.12860	4	B
16	10.1111/jonm.12758	4	B	81	10.1111/jonm.12773	4	A
17	10.1111/jonm.12891	4	A	82	10.1111/jonm.12809	3	A
18	10.1111/jonm.12811	4	B	83	10.1111/ijn.12812	3	B
19	10.1111/nhs.12629	4	A	84	10.1111/jan.14252	3	B
20	10.1111/jnu.12498	4	C	85	10.1111/jnu.12534	4	A
21	10.1111/nuf.12374	4	A	86	10.1111/jan.14204	4	A
22	10.1111/nuf.12407	4	A	87	10.1111/jonm.12872	3	B
23	10.1111/wvn.12402	2	B	88	10.1111/ajr.12513	4	A
24	10.1111/scs.12753	4	B	89	10.1111/jan.14016	3	A
25	10.1111/jocn.14990	4	B	90	10.1111/phn.12679	4	A
26	10.1111/jan.14047	3	A	91	10.1111/nup.12281	3	A
27	10.1111/wvn.12411	2	A	92	10.1111/nhs.12659	2	B
28	10.1111/jocn.14855	4	A	93	10.1111/jan.14176	3	A
29	10.1111/jonm.12894	3	A	94	10.1111/jan.14268	2	B
30	10.1111/jnu.12525	4	A	95	10.1111/phn.12650	4	A
31	10.1002/hec.3886	4	A	96	10.1111/nuf.12376	4	A
32	10.1111/jpc.14410_76	3	A	97	10.1111/nup.12257	4	A
33	10.1002/9781119439165.ch10	3	A	98	10.1111/scs.12728	4	A
34	10.1002/hec.3922	4	A	99	10.1111/nuf.12367	1	A
35	10.1002/nop2.270	4	A	100	10.1111/jonm.12907	4	B
36	10.1111/jocn.15046	4	B	101	10.1111/opn.12259	4	C
37	10.1111/j.1750-4910.2019.tb00045.x	4	A	102	10.1111/jonm.12878	1	B
38	10.1111/jocn.14968	4	A	103	10.1111/jocn.15073	4	A
39	10.1111/ijn.12798	3	A	104	10.1111/opn.12293	4	A
40	10.1111/phn.12595	4	A	105	10.1111/ajag.12758	4	C
41	10.1111/nuf.12355	4	A	106	10.1111/jonm.12875	2	B
42	10.1111/jocn.15150	4	A	107	10.1111/jocn.15177	4	A
43	10.1111/jan.14041	3	B	108	10.1111/jnu.12514	4	A
44	10.1002/hec.3924	4	A	109	10.1111/2047-3095.12265	3	A
45	10.1111/nhs.12627	3	A	110	10.1111/nup.12262	4	A
46	10.1002/ncp.10405	4	A	111	10.1111/nup.12282	4	A
47	10.1111/inr.12558	3	A	112	10.1111/nup.12277	3	A
48	10.1111/phn.12648	4	A	113	10.1111/nup.12283	4	A
49	10.1111/jonm.12841	4	A	114	10.1111/nup.12285	4	A
50	10.1111/jonm.12787	2	B	115	10.1111/nuf.12377	4	A
51	10.1111/nuf.12336	4	A	116	10.1111/nuf.12379	4	A
52	10.1111/inr.12529	2	A	117	10.1111/nup.12255	3	A
53	10.1111/jocn.14947	4	A	118	10.1111/nup.12284	4	A
54	10.1111/nuf.12412	4	A	119	10.1111/nuf.12375	4	A
55	10.1111/jocn.15105	3	B	120	10.1111/nup.12260	4	A
56	10.1111/nup.12241	4	A	121	10.1111/nup.12269	4	A
57	10.1111/jonm.12862	2	A	122	10.1111/ajag.12650	3	C
58	10.1111/jnu.12506	4	A	123	10.1111/inr.12496	3	A
59	10.1111/jonm.12765	4	B	124	10.1111/inr.12552	4	A
60	10.1111/nuf.12396	2	A	125	10.1111/j.1750-4910.2019.tb00043.xC	4	A
61	10.1111/nicc.12485	2	A				
62	10.1111/opn.12275	3	A				
63	10.1111/nin.12309	4	A				
64	10.1111/jonm.12853	2	A				
65	10.1111/inr.12518	4	A				

Year 2019							
#	DOI: https://doi.org/	Topics (1-4)	Fields (A-C)	#	DOI: https://doi.org/	Topics (1-4)	Fields (A-C)
126	10.1111/nin.12315	2	A	167	10.1111/jonm.12914	4	A
127	10.1111/opn.12245	4	C	168	10.1111/nhs.12653	4	A
128	10.1111/inr.12546	4	A	169	10.1111/phn.12636	4	A
129	10.1111/nin.12296	4	A	170	10.1111/scs.12635	4	A
130	10.1111/nuf.12372	4	A	171	10.1002/hpm.2767	2	A
131	10.1111/wvn.12412	4	A	172	10.1111/ggi.13816	4	A
132	10.1111/wvn.12414	4	A	173	10.1111/jan.14155	4	A
133	10.1111/inr.12543	4	A	174	10.1111/jnu.12463	4	A
134	10.1111/jan.13991	2	B	175	10.1111/jnu.12483	4	A
135	10.1111/jocn.14786	4	A	176	10.1111/jocn.14977	4	A
136	10.1111/jonm.12937	2	A	177	10.1002/cprt.30479	4	A
137	10.1111/nuf.12339	3	B	178	10.1002/nop2.240	2	A
138	10.1111/opn.12225	3	C	179	10.1002/nop2.262	4	A
139	10.1111/inr.12502	4	B	180	10.1002/nop2.271	2	A
140	10.1111/jocn.15082	3	A	181	10.1002/nop2.306	4	A
141	10.1111/jonm.12750	4	A	182	10.1002/smi.2907	2	A
142	10.1111/jonm.12846	4	A	183	10.1016/j.jalz.2019.06.2923	4	A
143	10.1111/nhs.12671	2	A	184	10.1111/1475-6773.13112	3	C
144	10.1111/opn.12256	2	A	185	10.1111/bcp.14101	3	C
145	10.1002/nop2.268	3	A	186	10.1111/bioe.12586	4	C
146	10.1002/nop2.281	4	A	187	10.1111/coep.12433	4	A
147	10.1002/nop2.404	4	A	188	10.1111/ggi.13631	4	C
148	10.1002/nop2.405	4	A	189	10.1111/hsc.12723	4	A
149	10.1111/jocn.14775	4	A	190	10.1111/ijn.12725	4	A
150	10.1111/jonm.12814	2	B	191	10.1111/ijn.12754	2	B
151	10.1111/jonm.12831	3	B	192	10.1111/ijn.12767	2	B
152	10.1111/jonm.12874	4	A	193	10.1111/inm.12572	2	A
153	10.1111/jonm.12887	4	A	194	10.1111/inm.12606	2	C
154	10.1111/nuf.12416	4	A	195	10.1111/inr.12560	2	B
155	10.1002/nop2.299	4	A	196	10.1111/inr.12571	4	A
156	10.1002/nur.21927	4	A	197	10.1111/j.1750-4910.2019.tb00041.x	4	A
157	10.1111/jan.13997	3	A	198	10.1111/jan.13972	4	A
158	10.1111/jan.14033	2	A	199	10.1111/jan.14049	3	A
159	10.1111/jocn.15155	4	A	200	10.1111/jan.14101	2	A
160	10.1111/nin.12293	4	A	201	10.1111/jan.14224	4	A
161	10.1111/nup.12289	4	A	202	10.1111/jan.14266	2	A
162	10.1111/scs.12731	3	C	203	10.1111/jan.14270	4	A
163	10.1111/inr.12528	4	A	204	10.1111/jjns.12277	2	A
164	10.1111/iwj.13174	1	A	205	10.1111/jnu.12520	4	A
165	10.1111/jan.13946	4	A	206	10.1111/jocn.14792	2	A
166	10.1111/jonm.12863	4	B	207	10.1111/jocn.14839	4	A

Year 2020							
#	DOI: https://doi.org/	Topics (1-4)	Fields (A-C)	#	DOI: https://doi.org/	Topics (1-4)	Fields (A-C)
1	10.1111/jnu.12606	4	A	66	10.1111/dme.14317	3	C
2	10.1002/nop2.652	2	B	67	10.1111/nin.12384	3	A
3	10.1111/nuf.12515	4	A	68	10.1111/jocn.15307	2	A
4	10.1111/jonm.13148	3	B	69	10.1111/dth.14396	1	A
5	10.1111/2047-3095.12301	4	A	70	10.1002/brb3.1837	2	A
6	10.1111/inr.12632	4	A	71	10.1111/ppc.12666	2	B
7	10.1111/jgs.16661	3	C	72	10.1111/jocn.15347	1	A
8	10.1111/jgs.16787	4	C	73	10.1002/emp2.12210	4	B
9	10.1111/jgs.16689	4	C	74	10.1111/jocn.15504	4	B
10	10.1002/nop2.576	4	A	75	10.1111/ggi.13934	4	C
11	10.1002/nop2.674	2	A	76	10.1111/jnu.12587	4	A
12	10.1111/jonm.13194	4	A	77	10.1111/spol.12645	4	C
13	10.1111/jonm.13121	2	A	78	10.1111/ppc.12555	2	A
14	10.1111/jocn.15520	2	A	79	10.1111/nup.12311	4	A
15	10.1111/jgs.16847	1	A	80	10.1111/nup.12314	4	A
16	10.1111/inr.12609	4	A	81	10.1111/jocn.15298	4	A
17	10.1002/nop2.616	2	A	82	10.1111/jgs.16520	4	C
18	10.1111/jonm.13168	2	A	83	10.1111/head.13811	1	A
19	10.1111/ppc.12661	2	A	84	10.1111/jgs.16765	4	C
20	10.1111/jonm.13094	2	A	85	10.1111/jocn.15315	4	A
21	10.1111/jocn.15553	2	A	86	10.1111/jocn.15297	4	C
22	10.1111/inm.12796	2	A	87	10.1111/jpm.12662	2	A
23	10.1111/jgs.16869	4	C	88	10.1111/phn.12733	4	A
24	10.1111/nicc.12528	2	A	89	10.1111/jgs.16687	4	C
25	10.1002/nop2.580	3	B	90	10.1111/jnu.12570	4	B
26	10.1111/jonm.13181	4	A	91	10.1111/inm.12800	2	B
27	10.1111/jonm.13095	4	A	92	10.1111/jocn.15322	4	A
28	10.1111/jan.14562	4	A	93	10.1111/jpm.12666	3	B
29	10.1002/emp2.12137	4	A	94	10.1111/jgs.16780	4	A
30	10.1111/inm.12775	2	A	95	10.1097/jnc.0000000000000173	4	A
31	10.1111/jonm.13124	2	A	96	10.1111/nup.12311	4	A
32	10.1111/jonm.13195	4	A	97	10.1002/nur.22056	4	A
33	10.1111/phn.12812	4	A	98	10.1097/ncq.0000000000000523	3	A
34	10.1111/jocn.15464	4	A	99	10.4103/nms.nms_40_20	2	A
35	10.1111/jgs.16784	4	C	100	10.1186/s13054-020-03160-6	3	A
36	10.1111/jocn.15454	2	A	101	10.1016/j.mnl.2020.07.011	4	A
37	10.1111/inr.12598	2	A	102	10.24843/JBN.2020.v04.is01.p06	3	B
38	10.1111/inr.12608	4	A	103	10.5334/aogh.2898	3	A
39	10.1111/ppc.12676	3	A	104	10.1111/onm.13148	3	B
40	10.1111/jan.14642	2	A	105	10.1016/j.nurpra.2020.10.034	4	C
41	10.1111/inr.12593	1	A	106	10.1016/j.mnl.2020.04.008	4	A
42	10.1111/ppc.12597	2	A	107	10.3390/ijerph17218126	2	A
43	10.1111/ppc.12648	2	A	108	10.1016/j.mnl.2020.08.011	4	A
44	10.1002/nop2.604	2	A	109	10.1089/tmj.2020.0089	3	B
45	10.1111/jonm.13014	2	A	110	10.1111/jnu.12606	1	A
46	10.1111/jonm.13122	2	A	111	10.2139/ssrn.3566190	4	A
47	10.1111/jocn.15548	2	A	112	10.1016/j.hrtlng.2020.04.021	4	A
48	10.1111/inr.12623	4	A	113	10.1111/jocn.15520	2	A
49	10.1111/jocn.15489	3	B	114	10.1016/j.profnurs.2020.06.008	3	A
50	10.1002/hast.1110	4	A	115	10.1111/tbj.14034	3	B
51	10.1111/jnu.12589	1	A	116	10.1097/01.numa.0000694872.75776.5b	4	A
52	10.1111/jocn.15444	2	A	117	10.1097/hnp.0000000000000395	4	A
53	10.1111/eve.13399	2	A	118	10.1111/jonm.13181	3	A
54	10.1111/nuf.12509	4	A	119	10.1016/j.jcjd.2020.04.002	4	A
55	10.1111/jocn.15549	2	A	120	10.1016/j.mnl.2020.07.008	4	A
56	10.1111/phn.12776	4	A	121	10.1080/24694193.2020.1757311	4	A
57	10.1111/ppc.12590	2	A	122	10.1097/ncc.0000000000000864	1	B
58	10.1111/jonm.13126	4	B	123	10.1016/j.nurpra.2020.10.004	3	A
59	10.1111/ppc.12601	2	A	124	10.1111/jocn.15347	2	A
60	10.1002/nop2.628	2	B	125	10.1136/bmjqs-2020-011512	4	B
61	10.1111/phn.12796	4	A				
62	10.1111/jocn.15469	2	A				
63	10.1111/ppc.12636	2	A				
64	10.1002/nur.22025	4	A				
65	10.1111/ppc.12678	2	A				

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#	DOI: https://doi.org/	Topics (1-4)	Fields (A-C)	#	DOI: https://doi.org/	Topics (1-4)	Fields (A-C)
126	10.1097/MD.0000000000020769	2	A	167	10.1111/jgs.16687	4	A
127	10.1016/j.bjoms.2020.07.033	1	B	168	10.1177/0969733016648205	4	B
128	10.1186/s13054-020-2841-7	1	A	169	10.1037/t60852-000	2	B
129	10.1016/S2215-0366(20)30168-1	2	A	170	10.1007/s12603-020-1401-9	3	C
130	https://doi.org/10.1136/bmj.m1211	2	A	171	10.1111/jgs.16780	3	C
131	10.1111/JOCN.15257	3	A	172	10.1002/AJIM.23144	1	A
132	10.1093/JAMIA/OCAA067	3	A	173	10.1111/INR.12578	4	A
133	10.1001/JAMAHEALTHFORUM.2020.0369	4	A	174	10.1016/J.JAMDA.2020.06.010	4	A
134	10.1016/S2215-0366(20)30149-8	1	C	175	10.1002/HAST.1110	4	A
135	10.3892/ETM.2020.8646	2	A	176	10.1017/ICE.2020.1283	4	C
136	10.1111/JGS.16490	4	C	177	10.1002/nop2.576	3	A
137	10.3386/W27608	4	C	178	10.22605/RRH5976	3	A
138	10.1111/JOCN.15305	4	A	179	10.7326/M20-3234	1	A
139	10.1056/NEJMP2014811	4	C	180	10.1111/jan.14468	4	A
140	10.1111/JGS.16784	4	C	181	10.1111/jan.14407	4	A
141	10.1016/J.NEPR.2020.102807	4	A	182	10.1111/jpm.12639	2	A
142	10.1016/J.IJNURSTU.2020.103587	4	A	183	10.1111/jan.14526	4	A
143	10.1177/1527154420938707	4	C	184	10.1111/jgs.16861	3	C
144	10.1001/jama.2020.14709	4	C	185	10.1002/nur.22046	4	A
145	10.1016/j.jnn.2020.11.002	4	A	186	10.1111/jocn.15257	4	A
146	10.1016/j.mnl.2020.07.008	4	A	187	10.1111/wvn.12451	4	A
147	10.1016/j.jopan.2020.04.001	2	A	188	10.1111/jgs.16529	4	A
148	10.1177/0894318420946493	4	A	189	10.1111/jan.14508	2	A
149	10.24144/2077-6594.3.2020.208655	4	A	190	10.1111/jgs.16447	4	A
150	10.1016/j.nurpra.2020.05.003	4	A	191	10.1111/psyg.12594	3	C
151	10.1016/j.psychres.2020.113272	2	A	192	10.1111/jgs.16499	4	A
152	10.1016/j.jamda.2020.08.002	4	C	193	10.1111/imj.14966	4	A
153	10.4236/psych.2020.115048	2	B	194	10.1111/inr.12607	1	A
154	10.1111/jan.14418	4	A	195	10.1111/jrh.12447	4	B
155	10.1016/j.jad.2020.06.047	2	A	196	10.1016/J.OUTLOOK.2020.04.013	4	A
156	10.1111/ppc.12661	2	A	197	10.1016/J.JAMDA.2020.07.038	3	C
157	10.1111/inm.12796	2	A	198	10.1111/JGS.16765	4	C
158	10.1111/jgs.16689	4	C	199	10.1002/jdd.12328	3	A
159	10.1080/01612840.2020.1752865	2	A	200	10.1177/1077558720969318	4	A
160	10.1111/jgs.16832	4	C	201	10.1007/S12603-020-1447-8	4	A
161	10.1111/jgs.16625	4	B	202	10.18502/npt.v7i2.2728	4	B
162	10.1111/jgs.16661	4	C	203	10.3912/OJIN.Vol26No01PPT62	3	A
163	10.1111/jgs.16477	4	C	204	10.1590/1983-1447.2021.20200120	4	A
164	10.1080/01612840.2020.1819083	2	A	205	10.1590/SciELOPreprints.934	1	A
165	10.1017/S1041610220000897	4	C	206	10.1590/1980-265x-tce-2020-0213	3	A
166	10.1111/jgs.16658	4	C	207	10.1590/0034-7167-2020-0259	4	A

To summarise this project: The general idea behind this work is to assess — without the need for surveys that would further overburden frontline health care staff, i.e., nurses — by semi-quantitative (non-parametric) analysis, the impact of COVID-19 through bibliometric research with statistically processed data.

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2.4.2. Telecommuting and distance learning after COVID-19.

Forced by the restrictions imposed in the fight against COVID-19, teleworking and distance learning have developed enormously during the pandemic. It is true that the technology was ripe for this, but according to one forecast, up to 50% of the time workers are not at their place of work, representing an enormous inefficacy of office use. By the end of 2021 about 25%–30% of teleworking has been forecasted, with savings per worker under this modality estimated to be as high as US$ 11,000.[9]

As in the previous case and to maintain the same structure, the two congress presentations have been included, keeping their style and references as requested by the organizers of those meetings.

● Lessons After Covid-19: Advances in Science and Economics Through Remote Information and Communication Technologies.

This paper was presented at the Charles Institute of European Studies, 3rd International Conference on Social Entrepreneurship, Social Innovation and Business Research. (SESB-MARCH-2021), March 27-28, 2011. Barcelona. Vol 04, ISBN**:** 978-969-683-698-8. https://cies.education/proceedings/Issue 42.

Summary:

Quarantine and other mobility restrictions due to COVID-19 have provided the opportunity to develop ICT procedures for distance telecommuting and learning schemes. A significant number of scientific congresses, meetings or workshops can continue to be held virtually. In the case of research stays, they could remain virtual in most cases, incorporating small changes in the university's software for recording these activities.

Distance work also offers a solution to the shortage of health staff, especially nurses. As virtually all facilities have Health Information Systems (HIS) to manage data, and electronic records, it would be possible to alleviate the shortage of such staff and the difficulties of returning to full-time shift work, especially at certain periods of life such as pregnancy or older staff before retirement, through teleworking activities, based on a digital signature and a home computer connected to the HIS.

This virtual approach will help reduce pollution, save tuition fees, help reconcile family life, help students with disabilities, illnesses, distance limitations or who need more time due to handicaps, lack of language skills or other difficulties.

Telecommuting and learning in less developed regions could be reinforced by community learning or work points (publicly funded or through charitable contributions).

*Key words***:** Economic growth; Education and Economic Development; Technological innovation; Health; Welfare; Human Capital; Skills; Research Institutions; gender discrimination.

JEL Classification: I230; I250, J240, J280, J710, O320

Introduction:

Probably very few events in the recent history of humankind have had such an impact on society as the COVID-19 pandemic, affecting health, workforce, the economy, education, travel, leisure and more in over 200 countries. Coronavirus pandemic impacted on primary sectors such as agriculture, petroleum, and oil, in secondary sectors on declines in the manufacturing industry of up to 80% in some countries and activities, and in tertiary sectors as leisure and education (Nicola et al., 2020). Stock markets and oil prices collapsed, and some sectors of the economy, such as tourism, suffered a double-digit decline, while for other products or services — such as hand sanitizer, e-commerce, virtual events, cyber security, home alarms, and home fitness, among others — demand increased significantly (World Bank Group, 2020). Due to collective uncertainty and hysteria, some products disappeared from the stores in the early stages of the pandemic, with the notable example of toilet paper

[9] *https://globalworkplaceanalytics.com/work-at-home-after-covid-19-our-forecast (accessed on 22 April 2021)*

hoarding (Laato et al., 2020) Labour efficacy and working patterns changed (Mayhew & Anand, 2020). The pandemic caused hoarding, compulsive panic buying and it has even changed the scheduling of operating theatres and other planned health activities (Moletta et al., 2020; Nicola et al., 2020).

For the most visible and direct effects there are other indirect effects, both positive and negative. There have been consequences in recycling, increase in organic waste production and related procedures, but also a reduction of greenhouse gas emissions not seen in decades and a remarkable reduction of concentrations of Nitrogen Dioxide (NO_2) (Zambrano-Monserrate et al., 2020).

Is it possible to draw conclusions and learn lessons in the field of science, economy, and engineering from the pandemic? As the old saying goes, is this crisis also an opportunity for improvement?

What follows is a justification focused on the tertiary sector, in particular healthcare and higher education students, of why this ICT-enabled distance activity should not only not disappear after the pandemic, but should even grow, building on this unexpected momentum.

Data:

1. Cons

There are data on the negative impact of the situation in students and healthcare workers. Increases in indicators of anxiety, depression and suicide attempts among university students related to the COVID-19 pandemic have been reported. An early study in China with 7,147 respondents showed increases in indicators of mental dysfunction, and a negative correlation of social support with anxiety level ($P<0.001$)(Cao et al., 2020). In New York City, a study of 1,821 adult university students confirmed the findings of increased psychological distress with increased indicators of depression and anxiety linked to COVID-19; the anxiety indicators were higher in the case of family savings inability (greater than 5,000 US dollars. OR = 1.3; I 95% CI) (Rudenstine et al., 2021). Furthermore, it is striking that, according to a survey of 1,000 university students in Greece between 4–9 April 2020, almost a third accept and a fifth are open to conspiracy theories, even though they are in higher education institutions and are supposed to have a certain capacity to evaluate and follow scientific methodology and academic rigour (Kaparounaki et al., 2020).

There may be limitations of teaching staff in some universities to create effective distance learning programmes. Encoding and decoding learning processes may be affected in online education, but in a sample of 260 students, where the encoding and decoding process was found to be affected, students tended not to notice it due to their cost-effectiveness and comfort (Ahmed, 2018). Difficulties have also been reported in the monitoring and final assessment of students. (Sokolova et al., 2018).

Isolation implies lack of continuous live communication and university social life. Distance learning reduces development of conventional communication skills and nonverbal language. However, there is a process of adaptation, notoriously different among students and professors (Sobaih et al., 2020).

The psychological disturbances among healthcare personnel have been widely published. They related to the stressful situation, overload, and risk for infection, particularly in frontline staff (nurses) (Chen et al., 2020; Conroy et al., 2021; Fernandez et al., 2020; Guixia & Hui, 2020; Labrague & De los Santos, 2020).

2. Pros

ICTs are already available for distance learning and working. Therefore, it does not require the tremendous organisational effort that has been necessary in some other fields, e.g., to make the COVID-19 vaccine available in a few months. An early study (2 March and 14 April 2020) in a large health system (NYU Langone Health) demonstrated an increase in telemedicine visits from 102.4 daily to 801.6 daily. (683% increase) (Mann et al., 2020).

Distance learning offers economic advantages and access to people who cannot attend face-to-face academic courses, stages, congresses, or meetings. It may prepare family response to other natural events (McDermott & Cobham, 2012). The better educated are more able to cope with and adapt to the changes (higher levels of long-term resilience) (Frankenberg et al., 2013).
Telecommuting allows the incorporation of qualified personnel who are not currently working. For example, the shortage of nurses, a world-wide problem, is not so much linked to a lack of qualified staff as to a lack of planning mechanisms, poor retention and return policies, and inadequate professional career support (Buchan & Aiken, 2008; National League for Nursing, 2020; World Health Organization, 2016). The retirement need not be an on-off process, but a gradual progressive movement with increased activity from home.
Distance activities are also a barrier for other transmissible diseases. They improve the environment by reducing the greenhouse gas emissions, sound pollution, and the pressure on natural resources, such as forests, or beaches (Zambrano-Monserrate et al., 2020).

Discussion

There have been noticeable changes due to COVID-19 pandemic. Many publications have focused on the psychological aspects of staff, particularly health care workers and students. However, it is not clear that the changes could not be counterbalanced or incorporated into the natural process of adaptations normal in life evolution. It is true that psychological changes in healthcare workers have been reported (Huang & Zhao, 2020), but it is not so clear that the changes depend on home-working as "mood worsened regardless of whether work was in person or remote" (Conroy et al., 2021, p. 185). The natural tendency to adapt to change should not be forgotten. Faced with this, the system of remote activity offers unquestionable advantages. Part of the nursing shortage could be solved by telecommuting aspects such as constant patient monitoring, medication records and many other aspects that do not require face-to-face attendance and could provide opportunities for staff who, due to different circumstances, from pregnancy, breastfeeding, disability, chronic illness, or age, have the qualifications for the job, but not the availability to work face-to-face shifts including mornings, afternoons, and evenings.

In academia, informal communication between colleagues at an international congress or meeting is a very important element to consider and one that is hampered in remote proceedings. Some universities have found it difficult to adapt to the new distance learning situation. But distance teaching procedures have no time and distance barrier. It represents an economic saving in transportation, books, housing, fees, etc.

It is reasonable to think, especially if there are common educational spaces such as in Europe, that new distance programmes can be developed where subjects can be taken at different universities simultaneously, so that an academic curriculum can be tailored more closely to the student's aspirations and their future plans. On the other hand, loneliness and isolation is not restricted to students or telecommuting. It is a real problem of our society, specially affecting the elderly and that will require and independent approach (Tomstad et al., 2017). Social media is developing as a growing via of academic communication (Sobaih et al., 2020).

Remote technology may be reduced or unavailable in less developed and wealthy regions. However, this could be mitigated with new programs either with international support (UN or related agencies) or locally funded (tax or charity) to develop community teaching points where to connect during certain set periods, for a small or no fee .

Conclusions

Some are already claiming that the rapid development of distance teaching and working jeopardizes current working posts (Corbera et al., 2020), and it is certain that some labour changes will take place. But whether those changes will represent a reduction of work vacancies or rather a new reorientation for different skills is not so clear. The teleworking and distance

learning revolution will open up new possibilities, especially for disadvantaged students, who will be able to save money on transport, accommodation and textbooks, or for those living in non-urban, remote areas or at sea. For migrants with less knowledge of language, for workers (especially those with variable shifts that cannot be planned in advance), for pregnant women, and for those wanting to have time to care for their relatives, whether elderly or babies, for those deprived of their liberty, whether on a voluntary basis, such as religious community life, or serving a penal sentence. For the disabled, the elderly and the sick who need to be close to their treatment centres... and the list goes on and on. It also encourages independent development and self-learning. It is true that it reduces social life and communication, and that it makes final assessment and exam invigilation more difficult. But the current trend in exams is not towards a single test in a proctored room. There is a clear move towards continuous evaluation, where the assessment of what has been learned does not rely on good memory and luck on one day. There is no denying that there will be changes, adjustments, and annoyances, less renting lecture halls, and readjustments of spaces and staff. Nothing new in the social innovation cycle and in the constant shifting of market niches in the economic world of supply and demand.

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● New Approach to the International Doctorate.

This paper was presented in Spanish at the VI International Virtual Congress on Education in the 21st Century (14-28 April 2021), a meeting under the general theme on effects of COVID-19. What follows is an extract of the most relevant points included.

Abstract

Mobility restrictions due to COVID-19 have provided an opportunity to enhance Information and Communication Technology (ICT) procedures for remote telecommuting and education. A significant number of academic activities, such as scientific congresses, meetings, or workshops, could continue to be held virtually. The establishment of the virtual option is particularly advantageous in the case of research stays, which are required for the international mention of the doctorate. The design of these stays is outdated, as a large majority of activities could be replaced by distance meetings and other digital exchanges. The fact that prestigious centres, such as the University of Salamanca, following ministerial recommendations, have already opened up the option of doctoral defences and distance learning placements in response to the pandemic creates a precedent that will allow greater accessibility to the international mention of the doctorate.

This virtual approach has important benefits: it reduces tuition and accommodation and travel costs; it helps to reconcile family life; it benefits potential students with limitations due to disability, illness, restricted movement, or who require additional time due to language barriers or other difficulties. In addition, the reduction of travel has a positive impact on noise pollution and greenhouse gases.

Keywords: Doctoral studies, economic and educational development, technological innovation; research institutions, gender discrimination, disability, health, employment opportunities.

Complementary information extracted from congress presentation.

It is not necessary to have completed a third cycle of training to practise regulated professions. Occasionally there may be a requirement to have completed a third cycle of training, as this is required in certain cases, e.g., a doctorate for university lecturers, or a master's degree in legal practice for lawyers. However, even for state-regulated professions, such as medicine, nursing, or law, a doctorate degree is not required for professional practice. Nevertheless, the doctorate broadens the possibilities and prospects of the labour market, and despite the difficulties that further study in the postgraduate period may represent, it is an option pursued by many graduates. Moreover, as a result of the development of the European Education Area (EEA), international exchanges and the possibilities of finding a job in Europe have increased.

Within the EEA third cycle of education there is the possibility to complete a doctorate with international mention. This grew out of the so-called Rectors' Meeting, which first took the form of the Confederation of European Rectors' Unions and then merged into today's European University Association (EUA). The Association comprises more than 850 higher education institutions. In the field of knowledge promotion and exchange, the creation of a special recognition for doctoral degrees was envisaged for those who meet certain conditions. Upon fulfilment of these conditions, the candidate could apply for recognition of the European doctoral degree. The initiative has become a standard and has been developed, albeit unevenly, in different countries.

These programmes contribute to the creation of education and research networks, which in some cases have had a practical significance and multidisciplinary approach to emerging economies, as has happened in Latin America with the international doctorate in design and innovation that has been operating for almost two decades (Buono & Pelosi, 2013).

One of the requirements for a doctorate with international mention is to have spent more than three months in an accredited foreign research or teaching centre. However, the pandemic has seriously hampered this period of research, and the consequent expectations of doctoral students.

Its precursor was the European doctorate. The doctorate with a European mention was introduced at most universities following the corresponding agreements of the universities' governing bodies, based on higher education regulations, with the following requirements:

1/ The text of the doctoral dissertation must be written in a language customary for scientific communication in the field of knowledge, which cannot be that of the doctoral student's own university. Failing this, an important part of the text, at least the abstract, and some broad conclusions must be written in this language of scientific communication.

2/ A period of study or research work of more than three months in a prestigious foreign teaching or research centre is required. This stay must be endorsed by the Academic Committee, in agreement with the thesis supervisor.

3/ The thesis must have a report of aptitude for the international mention from at least two foreign PhD experts, which may not include the person responsible for the research at the foreign centre.

4/ The defence of the thesis must be conducted in a language of scientific communication, logically, in the same language in which it is written.

5/ There must be at least one member of the doctoral jury, with a doctoral degree from a foreign place, who may not be the same person in charge of the research stay.

Due to the autonomy of the universities, some aspects may change slightly, but always within these general requirements.

In Spain, the international mention, along with other aspects of doctoral studies, is regulated in RD 99/2011, of 28 January, which regulates official doctoral studies, published in the «BOE» no. 35, 10/02/2011, with subsequent modifications by RD 195/2016, of 13 May, published in the "BOE" no. 134, of 03/06/2016, which establishes the requirements for the issuance of the European Supplement to the University Degree of Doctor, modifying article 15 of the above-mentioned previous rule.

When the European mention regulations came into being, decades ago, technological development and the possibilities for distance work and training were very different from those of today, even more so given the boost they have received due to the Coronavirus pandemic. However, except in very specific cases where attendance is essential due to the need to be integrated into a clinical or animal research group, or for handling certain technical equipment, research does not require physical presence in a lab.

Given that most of the information is currently digitised, the analysis of this information can be carried out remotely, with the corresponding access codes. Regular meetings of the research team can be virtual, which does not preclude the exchange of images, presentations, and scientific discussions. E-mail and social networks with working groups significantly reinforce and complement this continuous flow of shared information.

Moreover, under RDL 21/2020, of 9 June, concerning urgent measures for prevention, containment, and coordination to deal with the health crisis caused by COVID-19 and related regulations, many university centres have developed options for telematic presentation and defence, with full legal validity. In addition, the Confederation of Directors of Doctoral Schools submitted a consultation to the Ministry of Universities in relation to stays for the international mention, with a positive recommendation.

In light of the above, this presentation proposed that international virtual stages should be generally valid, proposing changes to current regulations to adapt them to this new framework.

Reference (included in this extract)

Buono, M., & Pelosi, S. (2013). The International Doctorate in Design and Innovation: an innovative model for European-Mediterranean education and research. Strategic Design Research Journal, 6(1), 20–28. https://doi.org/10.4013/sdrj.2013.61.03

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Chapter 3
Discussion

The Coronavirus SARS-CoV-2 pandemic represents an abrupt rupture of a paradigm that was believed to be immutable, of a life of uninterrupted technological, economic and welfare progress, forcing unknown social changes and generating insecurities, behaviour of fear and rejection of abandoning the previous way of life, even with violent street demonstrations (Pacho, 2020).

This pandemic has shown that society was not only unprepared for an unexpected intentional infectious contamination, such as in a war or bacteriological terrorist attack, but that it was also not prepared to face a pandemic, of which there have been previous historical precedents that should have served as a lesson.[10]

Health information systems were unable to absorb the data, despite increased efforts, and the information was inconsistent, creating difficulties for health planning and allocation of economic resources.

Thanks to the health economics methodology, an estimation of these data has been obtained in this research. It was clear from the outset that it would not be possible to obtain precise information. However, health management rarely requires data of absolute precision, which is in any case virtually impossible given the human nature of disease, but rather a range of values that are sufficiently accurate to be able to establish health forecasts.

The set of papers in the set of this thesis were developed parallel to the development of the pandemic.

The first article sought to establish navigational charts for healthcare managers. From the beginning, we considered that the mortality figures reported did not correspond to reality (as expressed in paper one), something that had already been suggested by the funerary association (AESPROF [Spanish Funeral Home Associaton], 2020) and finally recognised by the authorities, through the National Institute of Statistics (Instituo Nacional de Estadística (INE) [National Institute of Statistics of Spain], 2020).

The requirement to consider only those confirmed by PCR testing was contrary to the reality of many cases of coronavirus deaths which were not included in the count as they did not have this verification.

As commented, according to data as of 10 December 2020, 13,036 cases were suspected of having died from COVID-19, bringing the total number of deaths to 45,684, which is 18,557 more than the figure provided by the health authorities in that period.

[10] According to the WHO-requested Independent Panel Report, released to the media at the time of going to press (12 May), the pandemic could have been avoided. See:
https://www.france24.com/en/europe/20210512-covid-19-catastrophe-could-have-been-prevented-says-expert-panel (accessed on 17 May 2021).

The aim of the *first publication* was to establish an estimate of the main magnitudes of the pandemic for Spain, and, if possible, to provide an answer to the questions:

1/ Will it be a single outbreak or several?

2/ How long will it last?

3/ What will the morbidity and mortality be?

4/ What resources will need to be devoted to the pandemic?

5/ Will the population need to be confined or can herd immunity be relied upon?

It was not possible to definitively answer the question of a single outbreak or not, but as suggested in the paper, considering the profile of the virus, the possibility of further outbreaks was introduced.

The issue of herd immunity was crucial as some governments (e.g., in the UK), were at the time considering the possibility of relying on herd immunity to avoid the economic and educational consequences of lockdown.

This point has important implications for work and education. The paper Covid-19 and school-age vaccination includes some data on the consequences, including the economic consequences of school closures, but how can such questions be addressed without reliable records?

To estimate answers to the above questions, a combination of methods was used. On the one hand, SARS-CoV-2, being an RNA virus, was estimated to behave in a similar time frame as other close viruses have behaved. The references used were those for MERS-CoV and influenza.

In addition, while the epidemiological data from the registers were of little use, they did serve to analyse trends and differential patterns. For example, even considering the limitations, early data suggested that mortality in Spain was higher than that reported in other studies.

The Best Adjustment of Related Values (BARV) method allowed a preliminary estimation of the basic epidemiological values needed.

This could be considered as a variant of meta-analysis, obtaining different variables in the form of ratios from different publications, and by applying those proportions to an absolute parameter —in this case the excess mortality in relation to the previous year— the other variables were computed. Here it was needed to assume *ceteris paribus* that all the excess of mortality recorded in 2020 as compared to 2019 was due to COVID-19.

The record of deaths is quite reliable and can also be verified indirectly through information from funeral homes, cemeteries, social security databases, etc. A first estimation was made and then an adjustment was sought so that the percentage errors were minimised in comparison with existing publications.

Once the epidemiological parameters had been estimated, the next step was to analyse the assessment of the role that herd immunity could play in the pandemic.

At the time of the estimation, an ongoing seroprevalence project (ENE-COVID, 2020) was already underway in Spain, involving more than 60,000 individuals of whom over 50,000 participated in the three rounds of the project. However, our estimate was made and published before the results of the ENE-COVID study were available. The reason for estimating a parameter for which much more reliable information would be attainable a few weeks later was to test the estimation method.

Although there was a difference of about 2.5% between the estimation published in paper one, and the seroprevalence reported in the study, the estimation showed that it was not

possible to rely on herd immunity, because, whether it was 2– 3% as forecasted in the paper or 5% as in the seroprevalence study, the figure was in any case far from the approximately 70% seroprevalence needed.

Consequently, the article met its objective of reasonable estimation of data and of rejection of natural herd immunity as a protective option against COVID-19.

♦

As the pandemic progressed, what seemed impossible, even to the eyes of experts, became reality, and vaccines were developed, tested, and made available in a record time that will undoubtedly go down in the history of Vaccinology.

Although it would not be true to say that no fake news has appeared before 2020, it is true that, probably due to insecurity and fear, which had already caused frenzied behaviours such as toilet paper hoarding, and the long hours of lockdown, the amount of fake news in relation to COVID-19 grew significantly and worryingly.

This is hardly new for the behavioural sciences, which have already recorded throughout history how in the face of extraordinary circumstances and whose consequences are not well known, doomsayers and false prophets of apocalypse emerge.

For this reason, in the second paper the advisability of establishing compulsory vaccination and the issue of facing fake news, were analysed, including whether it was possible or convenient to establish some kind of control over this non-scientific information.

The second lesson learned in relation to fake news focused on two very important aspects. Firstly, the fact that, on several occasions, disinformation was spread by professionals in the field of medicine, where truthfulness is considered to be very high. Ignoring the commitments made when started to practice the profession (Hippocratic Oath of ethics) and at odds with the code of ethics, some of these professionals published fake news which has caused enormous social damage.

Secondly, the lack of an adequate information policy for an action that should have been carried out jointly between the scientific world, the mass media, and the authorities, allowed the development of a growing current of fear of vaccination against COVID-19, which is, so far, the only hope of being able to acquire sufficiently large herd immunity to serve as a barrier to the spread of the virus.

As the *second publication* concludes, while establishing mandatory vaccination would be possible, perhaps supported by some additional reinforcing regulation to the existing legal framework, it was felt that other avenues should be exhausted before taking such a step. Suggestions included an adequate information campaign, something that has been shown to be clearly improvable, constituting an important lesson learned from this pandemic.

The obligation to show a vaccination certificate for selected activities such as entering certain premises, or for work, or for travel, could be a way that, while respecting the freedom of the individual, would encourage vaccination among the reluctant.

The negative tendency and fear, after the start of the vaccination campaign, has shifted. There was much less fear of the vaccine itself, but the fear was focused on the commercial brand. In this respect, the contradictory indications given for the AstraZeneca vaccine in a short lapse of time were of little help.

As far as controlling the spread of unscientific news, particularly that generated by health professionals, regardless of the actions that may be taken by professional associations (e.g., Medical or Nursing Colleges) against their members under the code of ethics, it seems that

the majority opinion based on statistical data prior to the pandemic is not to entrust such control to government authorities for fear of political manipulation.

This does not mean that social media should not strategically promote truthful information including the safety and efficacy of any vaccine approved for use by regulatory agencies across countries.

A large amount of vaccine-related misinformation was spread via social media aimed at risk-populations, especially with low health literacy and other groups who have not had the opportunity and/or the resources to develop the kinds of skills that are needed to assess the quality and credibility of information (Schiavo, 2020).

On the other hand, in a communication to the VI International Virtual Congress on Education in the 21st Century (14-28 April 2021), a meeting under the general theme on effects of COVID-19, the possibility of including children and pregnant women among the indications for vaccination was raised.

In the case of children, although it is true that their mortality is lower, when analysed in terms of quality-adjusted years of life lost this lower ratio reaches a much higher significance, which is why it is proposed that the child population also be considered when establishing vaccination plans.

♦

As this dissertation is focused on health economics, a *third publication* on cost analysis could not be left out and, as usual when a new treatment or prevention option is marketed, on its cost-effectiveness.

At this point in the research, when it was already clear that there would be several waves of the pandemic and it was beginning to be known that there would also be different strains of the virus, a first approximation was made of the healthcare costs and the cost-effectiveness of the vaccines.

The prices of the vaccines had not yet been published by then, so an estimate of the price was made, and the cost of the administration was taken from references of other vaccination plans plus an increase for the material for the extra protective measures.

A few estimates had already been published by then on the impact of the pandemic in economic terms, and the International Monetary Fund reported that if a policy of social distancing and other established measures were maintained, in monetary terms the pandemic could represent between 0.2 and 0.3 of the GDP of the previous year (2019) by 2020. Our estimate in this regard was 0.21% but based on the costs up to that date only, so the final estimated figure will be closer to 0.3% rather than 0.2%.

Even with the limitations of an estimate made amid the pandemic outbreak, the cost-effectiveness of the vaccine, as estimated in the paper, was very high (ICER of €5,132).

It should be noted, however, that the model did not consider the possibility of needing a regular annual vaccination schedule, or that new strains would behave significantly differently, or that vaccination would not be equally effective in this case.

♦

Without being part of the set of publications required for the thesis by published papers, additional research has been carried out to investigate the work climate in front line health care, i.e., nursing staff.

For this purpose, bibliometric methodology applied to general nursing publications was used. Publications on nursing specialities, and those relating to nursing procedures, were excluded unless they were related to COVID-19.

In this way, without the need for additional surveys of an already very saturated staff, it has been possible to confirm semi-quantitatively that the main shortcomings detected by clinical nursing staff, above all in primary care, have been those related to protection measures and psychological aspects (burn-out), while the data obtained from nursing staff in nursing homes points to the need to improve the organisational aspects of those facilities.

Another aspect analysed outside the set of publications was telecommuting and distance learning, both topics discussed in conference presentations.

The pandemic has notoriously brought about implementation of teleworking and distance learning. This (forced) initiative has open possibilities for the future. For example, as hospitals have computerised records, with most of the information digitalised, a significant part of nursing work, particularly that related to patient monitoring, could be done remotely.

It would facilitate the work of nurses who are on maternity or breastfeeding leave, as well as other groups such as the ageing workforce who often cannot keep up with morning, afternoon, and night shifts.

This is borne out, as it has been confirmed that there is not so much a shortage of qualified nursing staff, (i.e., trained staff), but of staff who are available for work. This same aspect of future development could also apply to other professions.

Distance learning will also be able to move forward thanks to the forced impetus that the pandemic has imposed. This could facilitate education for people in rural areas, people deprived of their liberty, people being treated for certain illnesses that limit their mobility (e.g., dialysis or chemotherapy), etc.

But we must not lose sight of the fact that there is a need to carry out certain activities collectively and that human beings are social and as such require social interaction for their integral development.

One example raised at the VI International Virtual Congress on Education in the 21st Century (14-28 April 2021) is the possibility, already implemented in some Spanish universities after consultation with the Ministry, of making the three-month stay required for the international mention of the doctorate virtual.

With proper controls, this process could greatly facilitate the higher level of the doctorate, i.e., the international mention, for doctoral students from distant places. In Spain in particular, it would increase the demand for this type of activity from future doctoral students from Latin America.

♦

To summarise, some of the most important challenges of the COVID-19 pandemic, including the lack or unreliability of data, the issue of mandatory vaccination, fake news, economic aspects such as the impact of the pandemic in terms of GNP and the cost-effectiveness of vaccines have been addressed in the research.

This information has been complemented by additional investigation, outside the set of articles, to review some other aspects such as the impact of COVID-19 in employment and education in order to obtain a more complete picture of the landscape and the challenges that society faces due to the pandemic.

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Chapter 4
Conclusions

The lessons learned from this research and the resulting publications can be summarised as follows:

1/ The monitoring and reporting systems (including Spanish) were not prepared for an outbreak of a pandemic of such magnitude. Neither were there appropriate preventive plans or sufficient stock of personal protection equipment.

2/ Information released was, consequently, inaccurate, erratic, and inconsistent, even though the greatest efforts made by those responsible must be acknowledged.

3/ These weaknesses had a critical impact on health economy and planning.

4/ The alternative approach used in this research, with mathematical models and other analyses including reviews of surveys, legal framework review, and bibliometrics, proved to be alternative paths for information procurement in such critical circumstances.

5/ The method of Best Adjustment of Related Values (BARV), used specifically to adjust related variables in a stepwise process, restricting their range based on those with more accurate precision, proved to be useful for estimations with enough precision for management purposes.

6/ Despite statements by some world leaders that COVID-19 was nothing but another flu process, the data obtained confirmed that, when compared to A-influenza, and with prevalence not very different at a set point, it required much more healthcare resources, causing collapse of ICUs and a dramatically higher mortality.

7/ Through indirect estimations (using BARV) it was possible to exclude the possibility of using herd immunity as barrier, something also initially considered by governmental authorities in some places (such as the UK).

8/ The confusion created by the COVID-19 outbreaks and the subsequent lockdowns increased the circulation of fake news, feeding conspiracy theories such as the role of 5G in the disease and created a growing suspicion about the safety and effectiveness of the vaccines. Furthermore, the vaccines have been developed with new methodology and in record time, adding contributing factors to the mistrust. However, looking at the core of public opinion, both before and after the pandemic outbreak, while it recognises that fake news creates confusion, undermines democracy, and should be acted upon, there is no majority support in those surveyed for government action on this.

9/ Although it seems possible to find a legal route for compulsory vaccination, it seems that support for this idea would not be overwhelming either.

10/ Analysing the data as of 17 February 2021, it is estimated that Spain, taking into account only direct costs, had spent about 50 euros per inhabitant and 0.21% of GDP on health care by the COVID-19.

11/ Vaccines, assuming at least 70% efficacy and the suggested market prices, seem to be very cost-effective, with an ICER for two doses per person at € 30 each (including administration), as of 27 October 2020, of € 5,132 (4,926 – 5,276) per QALY gained. This figure descends for every subsequent day of active pandemic.

12/ The labour climate in nursing has changed significantly with the appearance of COVID-19, as confirmed by a bibliometric review of a significative sample of nursing publications. Papers from general or hospital nurses reflect worries in issues related to barrier or protection measures, fatigue, psychological stress and in general resilience, while publications from nursing homes are mostly targeted at issues related to facility organization.

13/ The pandemic has boosted telecommuting and distance learning. Some of the aspects relating to this remote approach that were implemented by necessity could remain as advantageous for certain groups, both professionals who cannot do face-to-face work and students who can complement their training with distance methods.

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Style & Copyright

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As the final author editions, the articles included in this thesis have different formats and styles, resulting in an eclectic text. Nevertheless, it has been considered that in order to keep the texts as they have been published, it was not possible to adopt any other solution.

The *Manual of the American Psychological Association* (APA), Seventh Edition (2019) has been used as a complementary formatting-style source particularly for the part of the text and the corresponding references, but with some exceptions (e.g., no 5" indentation has been included in paragraphs, and also, tables and figures are not included after the references on separate pages, following APA recommendation, but again, intentionally, they have been embedded in the text, to facilitate reading. The double-space bibliography rule is also omitted. Text has been justified (both margins alignment). These points are intentionally not in accordance with the general recommendation in APA Manual. All these exceptions or changes have been consistently maintained. The references above this section correspond to that text only, and those already included in the sections of published articles have not been repeated.

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