 doi:10.20944/preprints202004.0470.v2

Title page

Type of Article: Mini Review

Title: EXPLORING URGENT NON-PHARMACOLOGICAL AND SOCIOECONOMIC INTERVENTIONS FOR THE COVID 19 EPIDEMIC IN SPAIN.

Running title: Non-pharmacological interventions for COVID 19

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Conflicts of interest: none.

Abstract:

Non-pharmacological interventions in the fight against COVID 19 include: a) suppression, which facilitates its extinction; and b) mitigation, which reduces its speed of spread. Left unmitigated, the intensive care unit bed capacity (ICU) is exceeded over its maximum supply, resulting in increased deaths. Suppression has shown in simulation models the potential for decreasing ICU occupation below its surge limit, effectively decreasing mortality. However, for avoiding a rebound in transmission, suppression must be maintained intermittently until a vaccine is available (which may take up to 2 years). The objective of this paper was to describe the mortality patterns observed in Spain, Italy and South Korea for discussing a hypothetical combined public health policy and socioeconomic model that could potentially reduce mortality while reducing the economic impact of this pandemic in Spain. The plan is based on a progressive-voluntary reinstatement to work of the population exposed to the lowest risks (healthy non-immune family units <50 y/o and immune population) and it depends on having sufficiently available ICU beds for providing adequate support. This model, if proven correct for Spain, could eventually be followed by other countries facing a similar impact of the present pandemic.

Keywords

Non-pharmacological interventions; COVID 19; health policy; mortality; economic; intensive care unit.

Abbreviations

NPI: non-pharmacological interventions; GB: Great Britain; US: United States of America; ICU: intensive care unit; Case fatality ratio (CFR); True Lethality Rate (TLR).

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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Introduction

There are two fundamental non-pharmacological interventions (NPI) in the fight against the COVID 19 pandemic[1]: a) suppression, which attempts to reverse epidemic growth below a level that facilitates its extinction; and b) mitigation, which attempts to reduce the speed of spread of the outbreak without extinguishing it. In a simulation model done at the Imperial College, Ferguson et al[1] compared the results from an unmitigated strategy (avoiding any NPI) versus the implementation of mitigation (case isolation, household quarantine and social distancing of the elderly) versus a suppressive strategy (social distancing of the entire population, case isolation, household quarantine and school and university closure) in Great Britain (GB) and in the United States of America (US).

In an unmitigated epidemic scenario, Ferguson et al[1] estimated that 81% of the population would be infected over the course of the epidemic and that the intensive care unit bed capacity (ICU) would be exceeded in GB by a demand over 30 times greater than its maximum bed supply, resulting in approximately 510,000 deaths in the GB and 2.2 million in the US. In a mitigated scenario, they expected that the surge limits for ICU beds would be exceeded by at least 8-fold, resulting in 250,000 deaths for GB and 1.1 to 1.2 million in the US. Suppression showed the potential for decreasing ICU occupation below its surge limit, resulting in their best strategy for decreasing mortality. However, for avoiding a rebound in transmission, suppression would be maintained for at least 66% of the time until a vaccine was available for immunizing the population – which could take 1.5 to 2 years[1]. Thus, suppression would require an "on / off" implementation, so that the entire population would be allowed to return to work (maintaining mitigation measures) each time the number of ICU weekly admission rates decreased below a value ("off" mechanism); whereas the entire population would be re-suppressed each time the ICU admission rate exceeded a value ("on"). The application of this method would generate "contained epidemic waves" until the entire population acquired immunity (possibly after around 50 to 80% of the population had been infected or vaccinated)[1].

The population of Spain, Italy and South Korea is fairly close in size (46.7, 60.5 and 51.2 million, respectively)[2]; however, these countries had shown different mortality rates during this pandemic at the time at which this manuscript was written (May 17th, 2020). Case fatality ratios (CFR) and total deaths had been much higher in Spain and Italy[3-5]. The objective of this paper was to describe the mortality patterns observed in Spain, Italy and South Korea for discussing a hypothetical combined public health policy and socioeconomic model that could potentially reduce mortality while reducing the economic impact of this pandemic in Spain.

Discussion

1. Methods applied in this review.

We descriptively studied the number of deceased patients, the number of confirmed infected cases and CFR (deaths due to coronavirus/ number of confirmed cases), based on the latest available data by age range published by the Ministries of Health of Spain[4], Italy[5] and South Korea[3] on May 11th, 2020 (Table 1). These countries were chosen for being well developed countries, with a population relatively similar in size to Spain but with different CFRs.

The Spanish prevalence of COVID 19 infections was estimated through antibody testing (IgG) by the Spanish Ministry of Science and Innovation on May 11th, giving a prevalence of 5.0% of the population and suggesting that, cumulatively, around 2,346,739 people had been infected. Based on this prevalence and on the CFR reported on May 11th in Spain (Table 2), we estimated the true lethality rate (deaths due to coronavirus/ estimated number of cases based on prevalence) that would have occurred in a hypothetical scenario where the entire Spanish population <50 y/o would have become infected after being allowed to restart work unsuppressed on May 11th, while the rest of the population (>50 y/o) was kept under suppression[6,7].

2. Description of the mortality patterns observed in Spain, Italy and South Korea.

The data collected on May 11th at the Spanish Ministry of Health[4], showed an overall 11.76% CFR. Data for age groups (Tables 1 and 2) showed a 0.4% CFR (288 deaths in 71,761 cases) for patients

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younger than 50 y/o. On May 11th, 2020, the Korean Center for Disease Control and Prevention[3], reported lower mortality rates than Spain (Table 1), with a 2.35% CFR and a 0.078% CFR in patients <50 y/o (5 deaths in 6,392 cases). Italy had presented their statistics[5] for the general population on May 7th, with mortality rates relatively similar to Spain: a 13.1% CFR and a 0.52% CFR in patients <50 y/o (312 deaths in 59,749 cases). Italy had also described that their health workers had much lower mortality rates, with a 0.33% CFR for all ages and a 0.037% CFR for patients < 50 y/o (5 deaths in 13,364 cases) (Table 1).

3. Mortality rate estimation if we had allowed the Spanish population <50 y/o becoming infected after May 11th: hypothetical scenario.

Assuming a 5% prevalence[7], the Spanish TLR on May 11th was of 114 deaths per 10,000 infected cases (26,744 total reported deaths in 2,346,739 estimated infections). Furthermore, on May 11th, only 1.54% of the deceased patients were <50 y/o (288 deaths <50 y/o out of 18,722 subtotal deaths); thus, by extrapolating this data, the approximate true lethality rate (TLR) in patients <50 y/o in the entire country would have been around 3 deaths per 10,000 cases (1.54% of the 26,744 total deaths over the 2,346,739 estimated infections reported in the country), which is a mortality rate 91 times lower than the expected TLR in our population >50 y/o (272.7 deaths per 10.000, in >50 y/o), if left exposed to the infection (Table 2). Therefore, for our hypothetical scenario, where the entire Spanish population <50 y/o would have become infected after being left unsuppressed, 8,228 patients would have been expected to die. However, herd immunity should theoretically be achieved after around 50 to 80% of the population had been infected which, in this hypothetical scenario, would have resulted in 4,114 to 6,582 deaths[1,6]. Finally, despite lacking specific data in Spanish active workers, Italy has reported a mortality 14 times lower than the general population in their health workers <50 y/o (Table 1). Since the overall CFR are quite similar for Spain and Italy, we hypothesize that similar mortality rates could possibly be observed in the Spanish working population <50 y/o if left exposed to the infection (resulting perhaps in under 470 deaths, theoretically). Further reductions in mortality could be achieved by exposing only the healthy population <50 y/o.

4. Importance of CFR and TLR in patients <50 y/o: implications for health policies.

Following Ferguson's model[1], decreasing ICU occupation below its surge limit, should result in the best strategy for decreasing mortality. In the following weeks after this manuscript was written, we expected to see Spain decreasing its ICU occupation below its surge limit[8]. Moreover, there was an intense ongoing debate for deciding how to implement further NPI. If we followed Ferguson's model[1], we risked inducing "contained epidemic" waves by applying an "on and off" suppression strategy to our entire society for up to 2 years. Each wave could increase mortality if ICU occupation raised above surge limit, and it could severely affect the economy.

There are some causes of death at an epidemic scale in our world that do not trigger suppression strategies. Road traffic accidents have been considered by the World Health Organization as a hidden global epidemic[9]. The 2018 motor-vehicle death rate[10] in Turkey and in Spain was 4.64 and 0.58 per 10,000 vehicles on the road per year, respectively. The CFR for Hepatitis A in adults[11] is around 1,8%, and the CFR for Influenza A[12] is somewhere around 0.1%. Despite this data, vaccination for Hepatitis A and Influenza A is not compulsory in most countries in the European Union[13]. Moreover, despite the previous death rates in the previous epidemic conditions, the population circulates by road vehicle freely, and no suppressive measures are routinely implemented for those infectious diseases. In Spain and Italy, the CFR for patients <50 y/o has been < 0.52%, which is lower than the one for Hepatitis A in adults. Furthermore, the Italian working-population in the health sector (potentially exposed to the highest viral loads) have shown a CFR <0.1% for patients < 50 y/o, which is similar to the one for Influenza A (Table 1).

Flaxman et al[6], in a study analyzing the impact of NPI in 11 European countries, estimated that there are orders of magnitude fewer infections detected than true infections, mostly likely due to mild and asymptomatic infections as well as limited testing capacity. For Spain, the Spanish Ministry of Science[7] estimated an average prevalence of 5.0%. Based on his data, we believe that the overall TLR for the entire Spanish population could possibly be much lower (114 per 10,000) than its CFR (11.76%). Moreover, for the population <50 y/o, we could be facing a lower TLR (3 per 10,000) than the annual mortality rate derived from driving in Turkey. Furthermore, based on the Italian experience in their health workers, we should also hypothesize that the TLR could even be much

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lower in the healthy actively working population <50 y/o (up to 14 times lower than in the general population <50 y/o), which would result in a TLR lower than the annual mortality rate derived from driving in Spain.

The Spanish population under 50 y/o currently represents 58.7% of the entire country's population[14], and it comprises 74% of the population under 65 y/o (which includes the working age population). Based on our discussion, we hypothesize (Figure 1) that a selective suppression of the population should further reduce the number of deaths and lessen the impact on the economy if, when having enough ICU beds available for our population:

1. We allowed the healthy non-immune family units with all members <50 y/o to return voluntarily to their work (or studies) under mitigating conditions for achieving herd immunity (without no longer suppressing them again). We would define "healthy patients" as the ones without risk factors[15] for developing a lethal form of infection (e.g.: diabetes, hypertension, cardiovascular disease, chronic respiratory disease, cancer, immunodepression and pregnancy). Further studies should detail these risk factors.
2. We allowed all the immune family units to return voluntarily to their normal daily activities under mitigating conditions (without no longer suppressing them again). The methods for determining immunity would depend on technology that should be deployed in the coming weeks (e.g. IgG detection).
3. Our state provided support to family units that had some non-immune members ≥ 50 y/o and/or unhealthy, but whose other members (<50 y/o, healthy, immune) were fit for voluntarily returning to work. Hotels, residences or duly qualified media could temporarily house these members at risk.
4. We allowed age ranges ≥ 50 y/o to return voluntarily to work, once we had achieved sufficiently safe herd immunity (e.g. 50 to 80%) for the population under 50 y/o[1,6].
5. We maintained suppressive measures in the population that did not match the above indications.

Under Ferguson's model[1], we would basically be exposing the entire population to the virus every time that the suppression is "off", which could translate into having epidemic waves with a 2.35% CFR (Korea) to 13.1% CFR (Italy). Moreover, under Ferguson's model[1], we would only allow full working conditions for 33% of time in the 24 months following the first epidemic peak (due to multiple re-suppressions). On the other hand, by selectively unsuppressing the population <50 y/o, our model could witness an expected mortality rate much lower than the one derived from exposing the entire population to the virus, and it could allow up to around 75% of our work force to resume work full-time (with no re-suppressions) once our ICU occupation dropped below its surge capacity and we had sufficient ICU beds for supporting our population at risk (possibly, in days or weeks after this manuscript was written).

Conclusions

Based on our analysis of the existing literature, we propose a combined public health and socioeconomic model that could theoretically seek to provide our decision makers in Spain with alternative tools to the ones that are being implemented at present for: quickly achieving immunity with the lowest possible mortality, while propping up the fall of our economy. The plan is based on a progressive-voluntary reinstatement to work of the population exposed to the lowest risks (healthy non-immune family units <50 y/o and immune population) and it depends on having sufficiently available ICU beds for providing adequate support. This model, if proven correct for Spain, could eventually be followed by other countries facing a similar impact of the present pandemic.

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Tables.

		Spain, May 11th			South Korea, May 11th			Italy, general population, May 7th			Italy, health workers, May 7th		
		Deceased patients	**Confirmed Infected cases**	**CFR**	**Deceased patients**	**Confirmed Infected cases**	**CFR**	**Deceased patients**	**Confirmed Infected cases**	**CFR**	**Deceased patients**	**Confirmed Infected cases**	**CFR**
Total		26,744	227,436	11.76%	256	10,909	2.35%	27,955	214,103	13.1%	79	23,925	0.33%
Age	0 to 9	2	829	**0.24%**	0	141	**0.00%**	3	1,642	**0.18%**			
	10 to 19	5	1,545	**0.32%**	0	598	**0.00%**	0	2,908	**0.00%**			
	20 to 29*	23	13,098	**0.18%**	0	3,019	**0.00%**	9	11,457	**0.08%**	0	2,517	**0.00%**
	30 to 39	61	22,056	**0.28%**	2	1,188	**0.17%**	54	16,189	**0.33%**	1	4,140	**0.02%**
	40 to 49	197	34,233	**0.58%**	3	1,446	**0.21%**	246	27,553	**0.89%**	4	6,707	**0.06%**
	50 to 59	605	41,897	**1.44%**	15	1,960	**0.77%**	993	38,399	**2.59%**	19	7,939	**0.24%**
	60 to 69	1,654	33,838	**4.89%**	37	1,358	**2.72%**	2,976	29,252	**10.17%**	40	2,496	**1.60%**
	70 to 79	4,529	32,189	**14.07%**	77	711	**10.83%**	7,849	31,627	**24.82%**	15	126	**11.90%**
	80 to 89	7,688	37,153	**20.69%**	122	488	**25.00%**	11,395	38,042	**29.95%**			
	90+	3,958	18,115	**21.85%**				4,430	16,978	**26.09%**			
	Sub-totals	*18,722*	*234,953*	***8.0%***	*256*	*10,909*	***2.35%***	*27,955*	*214,047*	***13.1%***	*79*	*23,925*	**0.33%**

Table 1. Case fatality ratio (CFR) distribution by age groups in the general population for Spain, South Korea and Italy. CFR = deceased patients / confirmed infected cases. *For the population of health workers in Italy, the lower age range studied was 18 to 29 y/o.

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		Spain, Ministry of Health, May 11th			True estimates for a 5% prevalence, May 11th		Expected deaths if entire country became infected
		Deceased patients n (%)	Confirmed Infected cases	CFR	Infections (n)	TLR /10,000	Deaths (n)
Total		26,744	227,436	11.76%	2,337,739	114	534,880
Age	0 to 49	288 (1.54%)	71,761	0.4%	1,372,253	3	8,228
	50 to 90+	18,434 (98.5%)	163,192	11.3%	965,486	272.7	526,652
	Sub-totals	*18,722* (100%)	*234,953*	8%			

Table 2. Estimation of the true number of infections and true lethality rate (TLR) / 10,000 population, for Spain on May 11th; and expected number of deaths if the entire country had become infected with our ICU occupation above its surge capacity. Data is calculated for a 5% prevalence, based on the data provided by the Spanish Ministry of Health on May 11th. Population for Spain in 2020 was 46,754,782 (58.7% were <50 y/o). Case fatality ratio (CFR) = deceased patients / confirmed infected cases.

Figures.

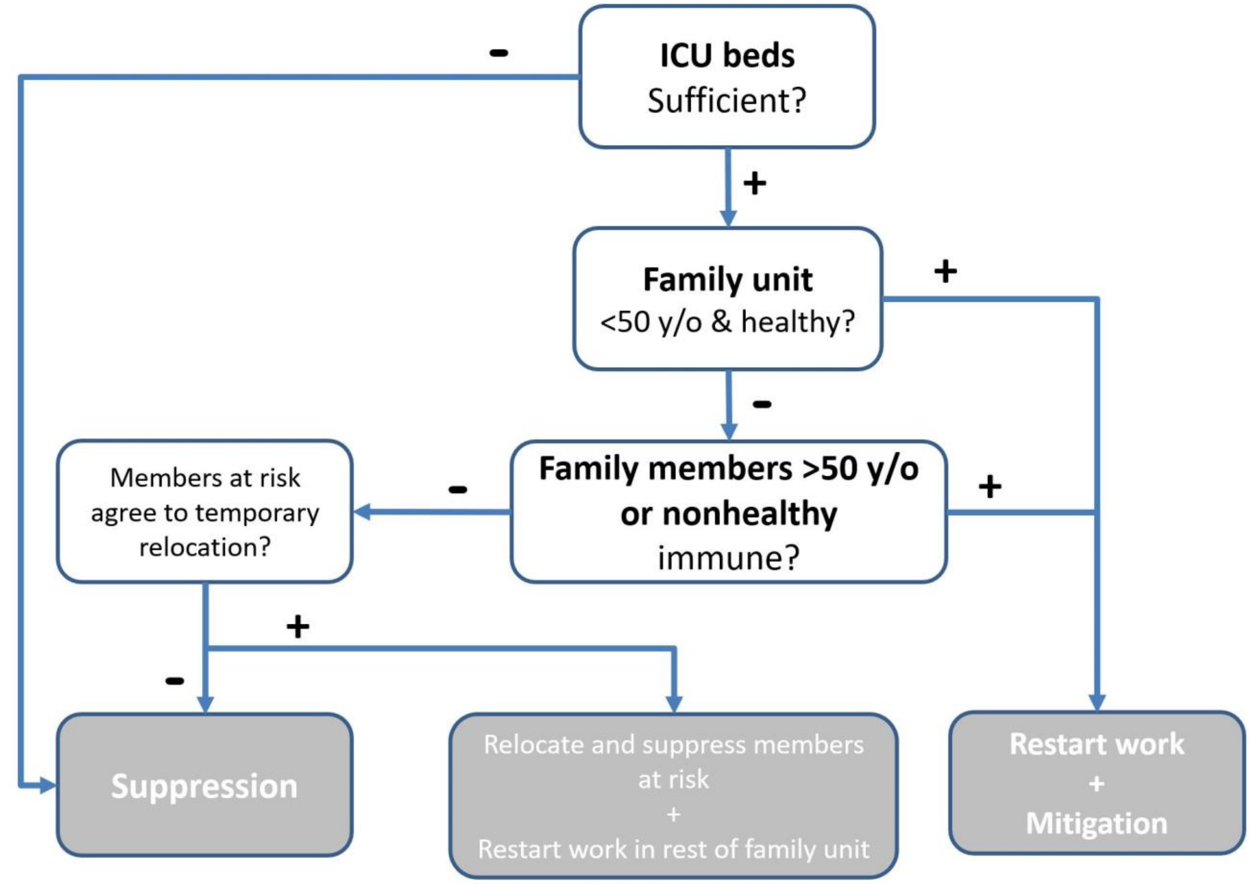

Figure 1. Flow diagram of a combined public health and socioeconomic model for policymakers for applying after the suppression of the first epidemic peak. The model would start its implementation when sufficient ICU beds were available (e.g.: 10 to 20% vacant). If all family members residing in the same location (family unit) were <50 y/o and healthy, they could restart work under mitigation. If some family members were >50 y/o or were tagged as "unhealthy" (diabetes, hypertension, cardiovascular disease, chronic respiratory disease, cancer, immunodepression and pregnancy), they could restart work under mitigation if they were already immune (due to previous confirmed infection and/or to thru IgG tests). If the family unit agreed to temporarily relocate their members at risk in safe environments supervised by the state (e.g.: hotels, etc..), the rest of the family unit could restart work under mitigation.