

COVID-19 and non-communicable diseases: systematic mapping of registered clinical trials



The George Institute undertook a systematic analysis of global COVID-19 related registered clinical trials by mapping how they relate to non-communicable diseases (NCDs). Our analysis outlines the current challenges, and provides recommendations about what we can do even better in the future.

What did we do?

Researchers from The George Institute for Global Health downloaded data on COVID-19 related clinical trials from the World Health Organization (WHO) International Clinical Trials Registry Platform on 29 June 2020 to identify registered interventional clinical trials. We coded the data to systematically map and understand the landscape of COVID-19 trials overall, and to analyse whether COVID-19 trials are addressing issues in intersection with NCDs. Primary outcomes were classified using the Cochrane EPOC criteria, with outcomes not covered under this classification clumped into a single category (i.e. Other). We classified countries based on the World Bank country classifications by income level (2019–2020).

What did we find?

1. A total of 2,108 interventional trials related to COVID-19 were registered for conduct in 93 countries or territories. There were 94 multi-country trials (4, 46.00%). China (371), United States (359), Iran (250), Spain (120) and France (107) had the greatest number of trials. The peak for registration of new trials was reached in April 2020 (812, 38.52%). A majority of the trials (1317, 62.48%) were described as investigating pharmaceutical products, with only 112 (5.31%) relating to behavioural educational and psychological interventions and only six trials (2.84%) relating to personal protective equipment (including face masks). Overall, only 309 (14.66%) trials looked at preventive aspects, outlined in Table 1.

Table 1 : Types of COVID-19 trials: Prevention Versus Management

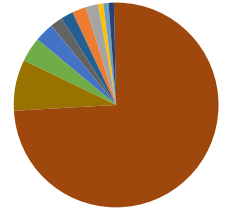
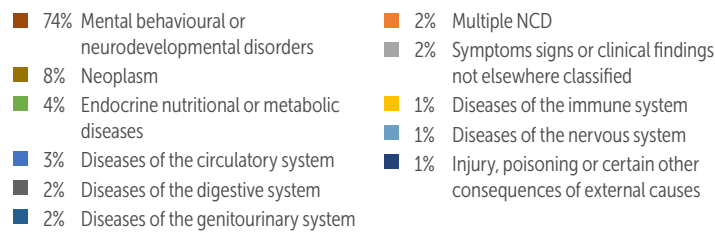
Type of trial	Number of trials	Percentage (%)
Management	1786	84.72
Others	13	0.62
Prevention	309	14.66
Grand total	2108	100.00

2. There are 109 trials (5.17% out of 2108) which are focused on NCD control as a consequence of COVID-19, of which 43 deal with prevention (39.45%), 64 with management (58.71%) and two on other aspects (1.83%). Most trials were conducted in the United States, Canada, China, Australia, and France, together accounting for 57 (52.29%) trials. There were no multi-country trials focusing on NCD control. Only one trial was from a lower middle income country (Honduras) and there were no low-income country led trials.
3. Analysis of these 109 trials on NCD control in the context of COVID-19 revealed:
 - The targeted sample sizes for these trials were:
 - o Less than 101 participants - 53 trials (48.62%)
 - o 101–1000 participants - 52 trials (47.76%)
 - o More than 1000 participants - 4 trials (3.67%)



- A large majority of the NCD control trials (74.00%) focused on mental behavioural or neurodevelopmental disorders, with only a few including other NCDs. This is outlined in Figure 1.

Figure 1: Trials on different types of NCDs in COVID-19 context



4. A large majority of these 109 trials focused on behavioural/educational or psychological interventions (66, 60.55%), followed by pharmaceutical interventions (17, 15.60%), traditional/alternative Medicine therapies (4, 3.67%) and several other interventions (22, 20.18%). Most of these trials (80, 73.39%) focused only on patient outcome as the primary outcome of interest with resource use, quality of care or access to services being scarcely being of primary interest. A detailed overview of primary outcomes in trials is presented in Table 2.

Table 2: Type(s) of primary outcome(s) for trial on NCD control in the context of COVID-19

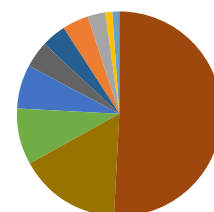
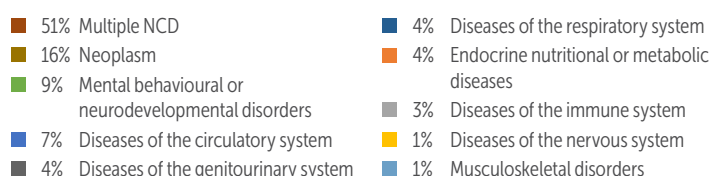
Type(s) of primary outcome(s) measured	Number of trials	Percentage (%)
Health care provider outcomes	9	8.26
Health care provider outcomes, social outcomes	1	0.92
Patient outcome	80	73.39
Patient outcome, adverse effects or harms	1	0.92
Patient outcome, health care provider outcomes	3	2.75
Patient outcome, others	2	1.83
Patient outcome, quality of care	3	2.75
Patient outcome, resource use	1	0.92
Quality of care	2	1.83
Quality of care, adverse effects or harms	1	0.92
Social outcomes, others	1	0.92
Social outcomes, quality of care	1	0.92
Utilisation or coverage or access	3	2.75
Utilisation or coverage or access, patient outcome	1	0.92
Grand total	109	100.00

5. There were 80 (3.79% of 2108 trials) trials focussing exclusively on people with COVID-19 and at least one on NCD as a co-morbidity. 70 (87.50%) of these trials focused on management aspects, with few addressing prevention (10, 12.50%). 19 of these trials were from the United States, with China and Spain both conducting six trials each. There are four multi-country trials, three of which were conducted in two countries (Lebanon and Israel; Austria and Germany; Austria and Denmark) and one in three countries (United States, Canada and Spain). Only two trials were from a lower middle income country (India and Nigeria) and there were no low-income country led trials.
6. Analysis of the 80 COVID-19 trials that focused on specific NCD populations revealed:
 - The targeted sample sizes for these trials were:
 - Less than 101 participants - 26 trials (32.50%)



- o 101–1000 participants - 41 trials (51.25%)
- o More than 1000 participants - 13 trials (16.25%)
- None of these trials have been completed and only 32 (40.00%) were actively recruiting at the time of data collection.
- Around half of these trials (51.25%) recruited participants from multiple NCDs, while some focused on COVID-19 in cancer patients (16.00%) or the mental health of COVID-19 patients (9.00%). The different types of NCDs included in these studies are shown in Figure 2.

Figure 2 : COVID-19 trials on specific NCD(s) population: Types of NCDs



7. The types of interventions and primary outcomes for COVID-19 trials on specific NCDs studied are shown in Tables 3 and Table 4 respectively. A majority of the trials focused on pharmaceutical products (58, 72.50%) assessing either patient (population) outcome and/or adverse effects as primary outcomes.

Table 3: Type of interventions investigated in COVID-19 trials on specific NCDs

Types of interventions	Number of trials	Percentage (%)
Behavioural educational and psychological	9	11.25%
Convalescent plasma	3	3.75%
Others	2	2.50%
Pharmaceutical medicine drug	59	73.75%
Stem cell	1	1.25%
Traditional/alternative medicine therapy/drug	4	5.00%
Vaccine	2	2.50%
Grand total	80	100.00%

Table 4: Type(s) of primary outcome(s) investigated in COVID-19 trials on specific NCDs

Types of primary outcomes	Number of trials	Percentage
Adverse effects or harms	1	1.25%
Adverse effects or harms, patient (population) outcome	1	1.25%
Patient (population) outcome	59	73.75%
Patient (population) outcome, adverse effects or harms	14	17.50%
Patient (population) outcome, quality of care	1	1.25%
Resource use	1	1.25%
Resource use, patient (population) outcome	1	1.25%
Utilisation or coverage or access	1	1.25%
Not reported	1	1.25%
Grand total	80	100.00%

What do these findings mean?

1. There is a need for global governance and priority setting around conduct of trials overall, to focus on several preventive aspects of pandemic control like the use of masks, chemoprophylaxis, behavioural educational and psychological interventions. The realignment of the clinical trial agenda away from the current heavy focus of pharmaceutical medicines and vaccines for COVID-19 affected patients is crucial.
2. Building an evidence base on preventive aspects of NCDs might be critical for economic recovery, as concerns about preventing outbreak



continue to remain. Currently, clinical trials are mostly focusing on clinical aspects of COVID-19, with few prioritising preventive aspects.

3. NCDs continue to have a high burden but only a few trials are looking at aspects of NCD control in the COVID-19 context. There is a need for building an evidence base as a consequence of COVID-19 but currently these studies are being conducted in only a few countries and in high income countries. Low and middle income countries which have high burden of NCDs have almost no trials. Currently trials are mostly looking at mental health conditions but understanding aspects of other NCDs is also required.
4. COVID-19 patients with NCDs are known to have high mortality. Yet there are only few trials specifically looking at these populations. More trials on this high-risk group are urgently needed. Most of the trials are looking at pharmacological outcomes and the need for studying non-pharmacological interventions is crucial. Most of the trials focused on patient (population) outcomes don't give much consideration to other important outcomes much consideration of other important outcomes such as social, quality of care, access to care outcome, which are key areas need to be addressed.
5. Most trials are conducted in individual countries. There is a need for international co-operation to prevent duplication of efforts and prevent research waste. Multi-lateral priority setting exercises, backed by governments, global institutions and global health funders, in an evidence approached manner with a wide range of stakeholders would be required for this purpose. COVID-19 also provides an opportunity to build an evidence base for preventive aspects of the pandemic, the window of opportunity for which still exists. Though challenging, this is an important aspect which needs to be studied. More funding for NCD specific COVID-19 trials and in control of NCDs in COVID-19 countries, especially in low- and middle-income countries is required.

Published Notes

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