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The landscape of COVID-19 trials in Australia

Anna Lene Seidler [1]
Research Fellow

Mason Aberoumand [1]

Jonathan G Williams [1]

Aidan Tan [1]

Kylie E Hunter [1]
Project Officer

Angela Webster [1, 2]

1. University of Sydney
   NHMRC Clinical Trials Centre
   Camperdown, NSW, New South Wales, Australia

2. Westmead Hospital
   Renal Medicine
   Westmead, New South Wales, Australia

Competing interests:

Anna Lene Seidler, Mason Aberoumand, Kylie Hunter and Angela Webster are affiliated with the Australian New Zealand Clinical Trials Registry (ANZCTR).

Anna Lene Seidler and Kylie Hunter are Associate Convenors for the Cochrane Prospective Meta-Analysis Methods Group.

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Introductory line:

Research response in Australia has been rapid, but better coordination is imperative.

Abstract:

This perspective explores the landscape of COVID-19 trials recruiting in Australia using trial registry data. We identified 56 trials addressing treatment and prevention of COVID-19, and 12 trials addressing indirect effects of the pandemic. Whilst there was substantial innovation in drug development and digital health, the potential of innovation in methodology, such as adaptive trials, remains largely untapped. Data sharing intentions were low, sample sizes were too small to detect differences in clinical outcomes, such as mortality, and lack of core outcome collection precludes evidence synthesis. Infrastructure for innovation would support coordination of research efforts, and reduce research waste.

Introduction

The coronavirus disease 2019 (COVID-19) pandemic has seen clinical trials launched at unprecedented speed in unprecedented numbers.(1) Whilst this is a positive development, the rapidity of trial launches and the unpredictable nature of the pandemic bring challenges for the conduct of trials and evidence synthesis. Duplication of effort is a risk and many trials alone are underpowered to find statistically significant effects for clinically important outcomes, including mortality.(1) Additionally, the 'hard-to-predict' waves of the pandemic may hinder recruitment due to declining cases, or pose challenges to starting trials quickly in emerging hotspots.(2) Recruitment has been a particular issue in Australia due to low case numbers compared with many other countries. In Australia, funds were made available rapidly to support research addressing the pandemic, but little is known about how effectively these funds have been utilised to drive the global agenda of preventing, diagnosing and treating COVID-19. We aimed to derive an understanding of the current landscape of clinical trials addressing the COVID-19 pandemic in Australia, and to what extent Australian researchers have responded to global need for coordination and collaboration.

Methods

We systematically searched the Australian New Zealand Clinical Trials Registry (ANZCTR) and ClinicalTrials.gov from 1st January to 16th November 2020, as these sources capture ~95% of registered trials recruiting in Australia.(3) We included all interventional studies addressing prevention, diagnosis and treatment of COVID-19 as *COVID-19 trials*, and all trials on indirect pandemic effects (e.g. lockdown measures, anxiety) as *COVID-19 related trials*. Observational studies were excluded. We analysed number and size of trials, additional recruitment countries, funding, trial purpose, study design, data sharing plans, and availability of core outcomes (mortality, respiratory failure, multiorgan failure, shortness of breath, recovery; Supplementary Table 1).(4)

Impressive research scale-up

Research scale-up in Australia during the COVID-19 pandemic has been impressive. Of 1,637 studies registered, 1,174 were interventional studies with a recruitment site in Australia. Of these, 56 were

COVID-19 trials, targeting 33,757 participants (Figure 1). Their characteristics are summarised in Table 1, with detailed information in Supplementary Tables 2a-c. Four of the trials (7%) were completed, the remainder were recruiting (n = 26, 46%), not yet recruiting (n = 24, 43%) or withdrawn (n=2, 4%, withdrawal reasons in Supplementary Tables 2a-c). The majority (46 trials, 82%) recruited only in Australia, whilst 10 trials (16%) recruited in Australia and internationally. Most (40 trials, 71%) had no commercial sponsor, and were funded by government or not-for-profit sources. Only 7 trials (12%) included populations at high-risk of poor outcomes from COVID-19 such as those with co-morbidities (e.g. cancer, cardiovascular disease, chronic kidney disease).

Nineteen (35%) were prevention trials. We identified 10 (18%) vaccine trials, of those, 2 (20% of vaccine trials) repurposed existing vaccines for COVID-19 prevention. Eight trials (80% of vaccine trials) investigated efficacy using a COVID-19-specific antigen. Thirty-four (62%) were treatment trials, 22 of those were (39%) drug trials. A broad array of drug categories was investigated, including but not limited to: immunosuppressants, immunostimulants, stem cell therapies, antivirals and anti-inflammatories. Merits, risks and proposed solutions of included trials are summarised in Table 2.

We identified 12 *COVID-19 related trials* (Table 1, Supplementary Table 3), and the majority (n = 11, 92%) addressed mental health issues related to uncertainty and isolation during the pandemic.

Fast-track procedures may have impacted scientific rigor and research prioritisation

The flipside to the rapid emergence of trials is the haste with which funding, development and implementation happened - leading to concerns about research waste and prioritisation, and ethical/scientific rigor.(5) Adding concern is the fact that no full, publicly available protocols were identified for any of the included trials. Most organisations did not have fast-track procedures in place at the start of the pandemic.(5) The development of publicly available, transparent procedures and standards for all stages of clinical trials (e.g. development, funding, ethics, conduct, dissemination) should be an important lesson from the current pandemic. Such standards must balance the urgency of advancing knowledge with the retention of ethical and scientific rigor.

The majority (89%) of included trials tested pharmaceutical drugs or devices, except for six trials: three telehealth applications for COVID-monitoring/ rehabilitation, one lifestyle intervention, and one intervention on patient positioning during oxygenation. There were no trials on public health communication, community transmission prevention or long COVID symptoms, pointing to omissions in research prioritisation. Additionally, extensive media coverage and public opinion may have influenced prioritisation of interventions that were not particularly promising.(1, 6) For instance, many simultaneous trials emerging on (hydroxy)chloroquine (six in Australia alone) may have put too many patients unnecessarily at risk.

Innovation in drug development and digital health, but potential of innovative study designs remains untapped

Australian COVID-19 trials tested a range of innovative interventions, such as vaccine techniques (nanoparticles and the delivery of genetic material in two vaccine trials) and digital health solutions for home-monitoring of mild COVID-19. Trialists demonstrated adaptability to transmission risks for in-person contact through innovation in trial conduct, with digital recruitment and delivery modes such as video-calls or smartphone applications. Yet, innovation in trial design was lacking. We identified only two trials utilising adaptive methods (Bayesian designs), which can respond to the rapidly changing landscape of treatment options, and thus deliver results more efficiently.

Trials often underpowered for clinical outcomes

The median target sample size was small (150, Q1-Q3=33-395), meaning that individually trials were likely underpowered to detect differences in clinically important outcomes.(4) For instance, to detect a 30% relative reduction in mortality (similar to that observed for corticosteroids(7)) with 80% power, one would need a sample size of 4,424 in a hospitalised population (with baseline mortality rates around 7% (8)) (Supplementary Figure 1). None of the identified treatment trials are sufficiently powered to detect such a difference in mortality, and with low case numbers in Australia it seems unlikely that a single trial could obtain such large sample sizes.

Limited collection of core outcomes precludes evidence synthesis

Evidence synthesis in the form of meta-analysis across trials is critical to obtain sufficient power to detect differences in core outcomes, or subgroups of participants, particularly when individual trials are underpowered. Core outcome sets were agreed early in the pandemic, and are evolving.(4) Of the 34 COVID-19 treatment trials in Australia, the proportion assessing each core outcome was low (Figure 2). For instance, only 53% (18 trials) assessed mortality, and 18% (6 trials) assessed shortness of breath, whereas 63% (21 trials) assessed respiratory failure. Only one trial included all core outcomes, and 10 trials (29%) included none. Thus, it will be impossible to synthesise results or make important comparisons for many of the trials.

Data sharing intentions low

The International Committee of Medical Journal Editors (ICMJE) declared data sharing an ethical obligation,(9) to honour the risk trial participants take by increasing the likelihood that their participation results in useful findings.(2, 9) Since the pandemic began, there have been several high-profile calls for collaboration and data sharing across studies, to enable more complex analyses and reliable effect estimates than would be obtained by simple combination of aggregate data.(2, 10) These calls seem to pass largely unheard among trialists in Australia, with 80% (41 trials) indicating they are not planning to share data (Table 3). Whilst these declarations at trial outset may be conservative and investigators may decide to share data later, they are still concerning. Frequently mentioned barriers to data sharing include a lack of understanding of the relevance, lack of resources to prepare data, insufficient academic recognition, and concerns about participant privacy, ethical approval and data misuse.(11) Structural support by funding bodies, research institutions, ethical committees, and journal editors are needed to address barriers and facilitate data sharing.(11) This could include a recognition system for collaboration and data sharing, and standardised moderated processes for data sharing, following FAIR (Findable, Accessible, Interoperable, Reusable) principles.(12) To date, no recognised FAIR data repository is available in Australia.(12)

Opportunities for strategic coordination and collaboration

As the COVID-19 pandemic evolves, clinical and societal need for research evidence will continue. There may be shifts in research focus as our understanding of COVID-19 grows, perhaps to ‘long COVID’ or other sequelae. Co-ordinating research efforts is a cost-effective, more reliable and timely way of achieving larger sample sizes and thus more impactful research evidence. Prospective meta-analyses and other next generation systematic review approaches provide suitable frameworks to coordinate such collaborative research efforts, and to align on key elements of study design, such as core outcomes.(13, 14) Internationally, researchers have begun applying these frameworks to the

pandemic,(2, 10) including an influential prospective meta-analysis evaluating corticosteroid treatment for COVID-19.(7)

In Australia, the COVID-19 pandemic has led to rapid changes in some processes including fast-tracked funding, ethical approvals, trial registration and publication.(15) Yet, too little has happened in creating infrastructure and funding for rapid collaboration, advanced adaptive methodologies and data sharing. In future, with adequate funding for technological innovation, clinical trial registries may play a key role in automatically connecting similar trials and facilitating collaboration. The COVID-19 pandemic presents a unique opportunity to improve collaborative infrastructure and methodologies, and advance future research across all health areas.

References:

1. Davis JS, Ferreira D, Denholm JT, Tong SY. Clinical trials for the prevention and treatment of COVID-19: current state of play. *Med J Aust*. 2020; 213: 86-93. 10.5694/mja2.50673.
2. Petkova E, Antman EM, Troxel AB. Pooling data from individual clinical trials in the COVID-19 era. *JAMA*. 2020; 324: 543-5. 10.1001/jama.2020.13042.
3. Askie L, Hunter K, Berber S, Langford A, Tan-Koay A, Vu T, et al. The Clinical Trials Landscape in Australia 2006-2015. Sydney: Australian New Zealand Clinical Trials Registry, 2017. https://www.anzctr.org.au/docs/ClinicalTrialsInAustralia2006-2015.pdf (Accessed April 2021).
4. Tong A, Elliott JH, Azevedo LC, Baumgart A, Bersten A, Cervantes L, et al. Core outcomes set for trials in people with coronavirus disease 2019. *J Crit Care Med*. 2020; 48: 1622-35. 10.1097/CCM.0000000000004585.
5. Bahans C, Leymarie S, Malauzat D, Girard M, Demiot C. Ethical considerations of the dynamics of clinical trials in an epidemic context: Studies on COVID-19. *Ethics Med Public Health*. 2021; 16: 100621. 10.1016/j.jemep.2020.100621.
6. Saag MS. Misguided Use of Hydroxychloroquine for COVID-19: The Infusion of Politics into Science. *JAMA*. 2020; 324: 2161-2. 10.1001/jama.2020.22389.
7. The WHO Rapid Evidence Appraisal for COVID-19 Therapies Working Group. Association Between Administration of Systemic Corticosteroids and Mortality Among Critically Ill Patients With COVID-19: A Meta-analysis. *JAMA*. 2020; 324: 1330-41. 10.1001/jama.2020.17023.
8. Dennis JM, McGovern AP, Vollmer SJ, Mateen BA. Improving Survival of Critical Care Patients With Coronavirus Disease 2019 in England: A National Cohort Study, March to June 2020. *J Crit Care Med*. 2020; 49: 209-14. 10.1097/ccm.0000000000004747.
9. Taichman DB, Sahni P, Pinborg A, Peiperl L, Laine C, James A, et al. Data sharing statements for clinical trials: a requirement of the International Committee of Medical Journal Editors. *Ann Intern Med*. 2017; 167: 63-5. 10.7326/M17-1028.
10. Ma Z, Liu J, Pan Q. Overwhelming COVID-19 Clinical Trials: Call for Prospective Meta-Analyses. *Trends Pharmacol Sci*. 2020; 41: 501-3. 10.1016/j.tips.2020.05.002.
11. Tan A, Askie L, Hunter K, Barba A, Seidler A. Willingness to share individual participant data, and barriers and facilitators to data sharing: a retrospective cohort study and cross-sectional survey. 2020; 9 Suppl 1. 10.1002/14651858.CD202001.
12. The International Consortium of Investigators for Fairness in Trial Data Sharing. Toward Fairness in Data Sharing. *N Engl J Med*. 2016; 375: 405-7. 10.1056/NEJMp1605654.
13. Seidler AL, Hunter KE, Cheyne S, Berlin JA, Ghersi D, Askie LM. Prospective meta-analyses and Cochrane's role in embracing next-generation methodologies. *Cochrane Database Syst Rev*. 2020. 10.1002/14651858.ED000145.
14. Seidler AL, Hunter KE, Cheyne S, Ghersi D, Berlin JA, Askie L. A guide to prospective meta-analysis. *BMJ*. 2019; 367: l5342. 10.1136/bmj.l5342.
15. Whitmore KA, Laupland KB, Vincent CM, Edwards FA, Reade MC. Changes in medical scientific publication associated with the COVID-19 pandemic. *Med J Aust*. 2020; 213: 496-9. 10.5694/mja2.50855.

Table 1. Characteristics of COVID-19 trials (n = 56) and COVID-19 related trials (n = 12)

Characteristic	**COVID-19 trials (n = 56)** number (%)	**COVID-19 related trials (n = 12)** number (%)	**Overall (n = 68)** number (%)
Total participants across trials *(sum)*	33,757	2,586	36,343
Participants per trial			
Median (Q1-Q3)	150 (33-395)	147 (94-280)	150 (37-395)
Mean (SD)	625 (1507)	215 (184)	551 (1374)
Trial status			
Not yet recruiting	24 (43%)	9 (75%)	33 (49%)
Recruiting	26 (46%)	3 (25%)	29 (43%)
Completed	4 (7%)	0 (0%)	4 (5.9%)
Withdrawn	2 (4%)	0 (0%)	2 (2.9%)
Trial phase[1]			
Phase 0	0 (0%)	1 (8%)	1 (2%)
Phase 1	17 (31%)	3 (25%)	20 (30%)
Phase 2	13 (24%)	1 (8%)	14 (21%)
Phase 3	4 (7%)	1 (8%)	5 (8%)
Phase 4	2 (4%)	0 (0%)	2 (3%)
Not applicable (e.g. not a drug trial)	18 (33%)	6 (50%)	24 (36%)
Recruitment country			
Australia only	46 (82%)	11 (92%)	57 (84%)
International (Australia and other country/countries)	10 (18%)	1 (8%)	11 (16%)
Purpose [1]			
Treatment: drug	24 (44%)	0 (0%)	24 (36%)
Treatment: other	10(18%)	9(75%)	19(28%)
Prevention: vaccine [2]	8(14%)	0(0%)	8(12%)
Prevention: other	11 (20%)	2 (17%)	13 (19%)
Other (e.g. diagnosis, education)	2 (4%)	1 (8%)	3 (5%)
Included population			
Confirmed COVID-19	34 (61%)	1 (8%)	35 (51%)
Healthy volunteers	14 (25%)	3 (25%)	17 (25%)
Healthcare professional	6 (11%)	2 (17%)	8 (12%)
Individuals at high risk for poor outcome	2 (4%)	6 (50%)	8(12%)
Population age			
Adult (18 - 65)	9 (16%)	1 (8%)	10 (15%)
Older adult (age>65)	2 (4%)	1 (8%)	3 (4%)
All ages	45 (80%)	10 (83%)	55 (81%)
Any blinding (personnel or participant)[1]			
Yes	19 (37%)	3 (38%)	22 (37%)
No	30 (63%)	5 (62%)	38 (63%)
Randomisation[1]			
Randomised controlled trial	44 (81%)	7 (58%)	51 (77%)
Non-randomised trial	10 (19%)	5 (42%)	15 (23%)
Trials utilising digital health solutions			
Yes	5 (9%)	12 (100%)	17 (25%)
No	51 (91%)	0 (0%)	51 (75%)
Commercial involvement (sponsorship, collaboration or funding)			
No commercial involvement	40 (71%)	9 (75%)	49 (72%)
Commercial involvement	16 (29%)	3 (25%)	19 (28%)
Population with co-morbidity			
Yes	7 (12%)	2 (18%)	9 (13%)
No	49 (88%)	9 (81%)	58 (87%)

[1] No information available for one (1) trial each for trial phase and purpose, seven (7) trials for blinding (optional registration field), and two (2) trials for study design. These trials were excluded from the analysis for these characteristics. One trial with a sample size of 30,000 was excluded from the sample size analyses.
[2] Two (2) vaccine clinical trials registered on the ANZCTR were recorded as 'Treatment' for the 'Purpose of the study' field.

Abbreviations: ANZCTR, Australian New Zealand Clinical Trials Registry; COVID-19, coronavirus disease 2019; IQR, interquartile range; n, number; SD, standard deviation.

Table 2. Merits, risks and proposed solutions for COVID-19 trials in Australia

	Merits	Risks/ Research Gaps	Proposed Solutions
Speed of response	• Rapid response to emerging pandemic	• Haste in funding, development and implementation may have jeopardised scientific and ethical rigor	• Develop protocols for fast-tracked procedures in emergency scenarios balancing rigor and urgency
Number of trials & sample size	• Impressive research scale-up, many trials being launched	• Most trials relatively small, limited statistical power to detect effects on clinically important outcomes (e.g. mortality)	• Consider evidence synthesis opportunities throughout trial conduct, facilitate collaboration & coordination to enable pooling of data and results
Core outcomes and evidence synthesis	• Core outcomes have been developed early in the pandemic to enable successful evidence synthesis	• Data sharing/ collaboration intentions are low • Low proportion of trials collecting core outcomes (e.g. only 53% assess mortality)	• Encourage and create infrastructure for collaboration (e.g. in prospective meta-analyses) through funding bodies and trial registries • Establish recognition system for collaboration and data sharing following FAIR principles
Innovation	• Range of innovative interventions (e.g. vaccine solutions & digital health solutions) balanced with re-purposing of existing treatments • Innovation in trial conduct (digital recruitment & delivery modes)	• Lack of innovation in trial design (e.g. only two trials using adaptive designs)	• Increased use of adaptive designs to respond to the rapidly changing evidence landscape
Types of interventions and populations studied	• Broad array of drug categories investigated	• Extensive media coverage and public opinion may have misled research prioritisation (e.g. too many hydroxycholorquine trials) • Few non-pharmaceutical trials & no trials on public health communication or community transmission prevention • Few trials included populations at high-risk of poor outcomes from COVID-19 such as those with co-morbidities	• Improve research coordination and prioritisation through infrastructure (e.g. funders, trial registries), to ensure variety of priorities are met and to avoid duplication of effort

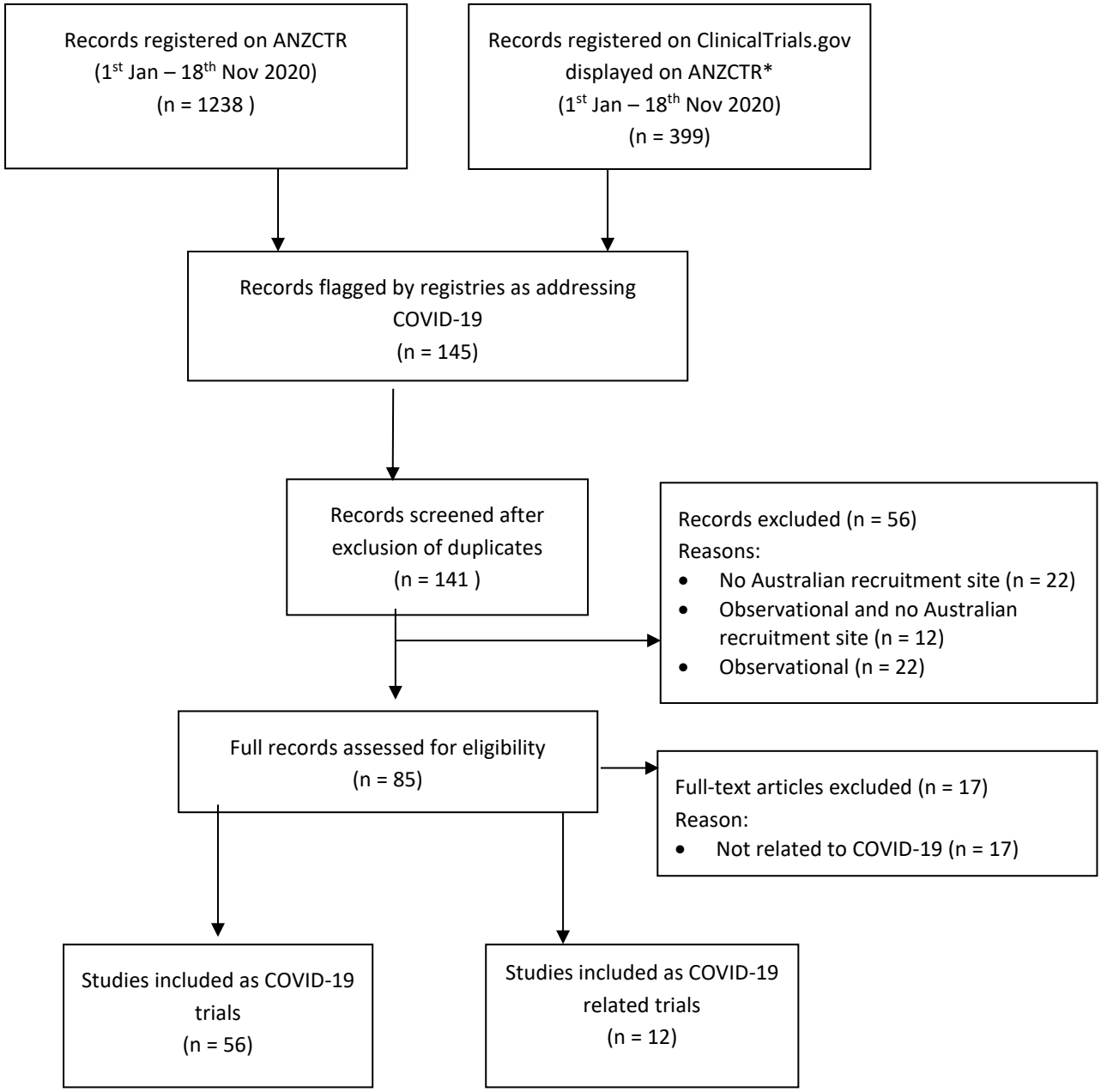
Abbreviations: COVID-19, coronavirus disease 2019; FAIR, findable, accessible, interoperable, reusable.

Table 3. Data sharing plans of COVID-19 trials (n=56) and COVID-19 related trials (n = 12)

	COVID-19 trials (n = 56) number (%)	**COVID-19 related trials (n = 12)** number (%)	**Overall (n = 68)** number (%)
IPD availability			
Planning on sharing IPD	10 (20%)	4 (36%)	14 (23%)
Not planning on sharing IPD	41 (80%)	7 (64%)	48 (77%)
No data sharing plan provided (excluded from percentage)	5	1	6
Reason for trials not planning on sharing IPD	n = 41	n = 7	n = 48
No reason	21 (51%)	3 (43%)	24 (50%)
Analyse aggregate data	7 (17%)	1 (14%)	8 (17%)
Undecided	5 (12%)	0 (0%)	5 (10%)
Protect participant privacy	3 (7%)	1 (14%)	4 (8%)
Lack ethical approval	2 (5%)	1 (14%)	3 (6%)
No external relevance	2 (5%)	0 (0%)	2 (4%)
Not data custodian	0 (0%)	1 (14%)	1 (2%)
Mechanism accessibility for trials sharing IPD	n = 10	n = 4	n =14
Principal investigator contact	7 (70%)	4 (100%)	11 (79%)
Primary sponsor contact	3 (30%)	0 (0%)	3 (21%)
Data repository	0 (0%)	0 (0%)	0 (0%)
Full protocol available	0 (0%)	0 (0%)	0 (0%)

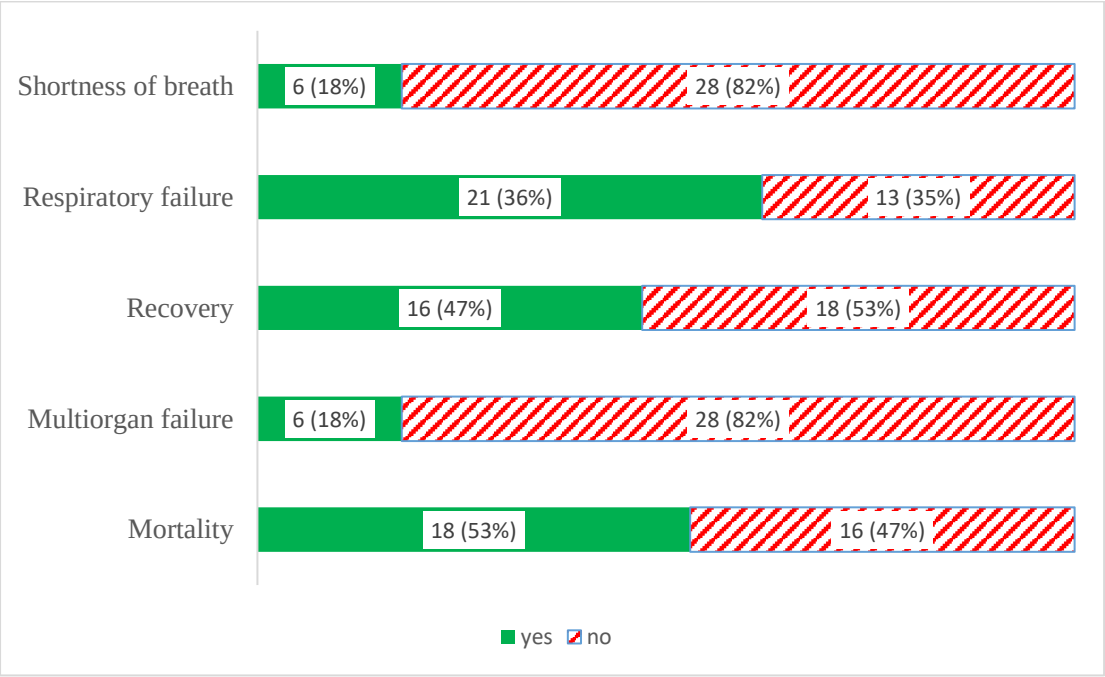
Abbreviations: COVID-19, coronavirus disease 2019; IPD, individual participant data n, number.

Figure 1. Flowchart of study selection



Abbreviations: ANZCTR, Australian New Zealand Clinical Trials Registry; COVID-19, coronavirus disease 2019; n, number.

Figure 2. Core outcome collection among 34 COVID-19 treatment trials (number, %)



Note: We only included COVID-19 treatment trials (n=34) in this analysis since we might not expect prevention or education trials, or trials on indirect effects of COVID-19 (e.g. mental health) to collect these core outcomes.
Abbreviations: COVID-19, coronavirus disease 2019.

Supplementary Table 1. Definition of COVID-19 Core Outcomes

Outcome	Definition
Mortality	Patient mortality; patient death; patient survival
Respiratory failure	Patient respiratory failure; patient need for intubation; patient need for mechanical ventilation; duration of patient intubation/ventilation; P/F ratio (arterial pO_2/ FIO_2) indicative of acute respiratory distress syndrome (ARDS) or respiratory failure
Multiorgan failure	Patient organ failure (other than lung); sequential organ failure assessment (SOFA) score; patient sepsis
Shortness of breath	Patient shortness of breath; dyspnoea; breaths/min
Recovery	Patient time to recovery; patient recovery; patient number of sick days; patient time to clinical improvement; duration of hospitalisation

Note: Core outcomes previously outlined (1), as defined for our study.
Abbreviations: COVID-19, coronavirus disease 2019; FIO_2, fraction of inspired oxygen; P/F, arterial partial pressure of oxygen/ fraction of inspired oxygen; pO_2, partial pressure of oxygen.

Supplementary Table 2a. Characteristics of included COVID-19 drug trials (n = 34)

Trial ID	Scientific title	Status	Sample size	Population	Co-morbidity	Drug type	Trial Purpose
NCT04567810	A Phase 1 Study in Healthy Participants to Evaluate the Safety, Tolerability, and Pharmacokinetics of Single -Ascending and Multiple Doses of an Anti-Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Chicken Egg Antibody (IgY)	Recruiting	48	Healthy volunteers	None	Intranasal anti-severe acute respiratory syndrome coronavirus 2 chicken egg antibody	Prevention: other
ACTRN12620001104943	A Phase 1, Placebo-Controlled, Single Dose, Escalating Dose Study to Determine the Safety and Tolerability of Intranasal REVTx-99 in Healthy Adult Volunteers	Not yet recruiting	32	Healthy volunteers	None	Intranasal REVTx-99	Prevention: other
ACTRN12620000816954	A Double-blinded, Randomised, and Placebo-controlled Safety Study of AT-301 Nasal Spray in Healthy Adults	Not yet recruiting	32	Healthy volunteers	None	Intranasal AT-301	Treatment: drug
NCT04532294	A First-in-Human, Randomized, Double-Blind, Placebo Controlled, Single Dose Escalation Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Immunogenicity of SARS-CoV-2 Neutralizing Antibody BGB-DXP593 in Healthy Subjects	Recruiting	30	Healthy volunteers	None	Intravenous SARS-CoV-2 neutralizing antibody BGB-DXP593	Other
ACTRN12620000834954	A Randomized, Double-Blind, Placebo-Controlled Study to Assess the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of Multiple Ascending Doses of GP1681 in Healthy Adult Participants	Not yet recruiting	24	Healthy volunteers	None	Oral GP1681	Treatment: drug

Trial ID	Scientific title	Status	Sample size	Population	Co-morbidity	Drug type	Trial Purpose
ACTRN12620000501943	Effectiveness of Prophylactic Hydroxychloroquine on incidence of COVID-19 infection in Front-line Health and Allied Health Care Workers: The COVID-SHIELD Trial	Recruiting	2250	Healthcare professionals	None	Oral hydroxychloroquine	Prevention: other
ACTRN12620000473965	Reducing acute severe respiratory events in health care workers during the Covid-19 pandemic with OM85	Recruiting	1000	Healthcare professionals	None	Oral OM85	Prevention: other
ACTRN12620000417987	Multi-Site, Randomized, Open-Label, Parallel-Group, Placebo-Controlled Study to Assess the Chemoprophylactic Efficacy of Chloroquine Against SARS-CoV-2/COVID-19 in Healthcare Workers at High-Risk of Exposure	Recruiting	680	Healthcare professionals	None	Oral chloroquine	Prevention: other
ACTRN12620000843954	COVID-19 Prevention and Treatment in Cancer; a Sequential Multiple Assignment Randomised Trial; C-SMART study. Arm 1: Effect of daily Interferon-alpha on cancer patients without known positive contact with COVID-19	Not yet recruiting	1914	Individuals at high-risk of poor outcomes	Neoplasm	Intranasal interferon-alpha	Prevention: other
ACTRN12620000842965	COVID-19 Prevention and Treatment in Cancer; a Sequential Multiple Assignment Randomised Trial; C-SMART study. Arm 2: Effect of daily Interferon-alpha on cancer patients with known positive contact with COVID-19	Not yet recruiting	170	Exposure to COVID-19	Neoplasm	Intranasal interferon-alpha	Prevention: other
ACTRN12620000588998	The safety and efficacy of STC3141 in patient with COVID-19 ARDS require intensive care	Withdrawn (recruitment difficulties)	160	Suspected/confirmed COVID-19	None	Intravenous STC3141	Treatment: drug
ACTRN12620000445976	Australasian COVID-19 Trial (ASCOT). A multi-centre randomised clinical trial to assess clinical, virological and immunological outcomes in patients with SARS-CoV-2 infection (COVID-19) treated with lopinavir/ritonavir and/or hydroxychloroquine compared to standard of care	Recruiting	2500	Confirmed COVID-19	None	Intravenous convalescent plasma [1]	Treatment: drug

Trial ID	Scientific title	Status	Sample size	Population	Co-morbidity	Drug type	Trial Purpose
NCT04483960	An International Multi-Centre Randomised Clinical Trial to Assess the Clinical, Virological and Immunological Outcomes in Patients Diagnosed With SARS-CoV-2 Infection (COVID-19)	Recruiting	2400	Confirmed COVID-19	None	Intravenous convalescent plasma	Treatment: drug
NCT04382924	A Randomized Open Label Phase 2b/3 Study of the Safety and Efficacy of NP-120 (Ifenprodil) for the Treatment of Hospitalized Patient With Confirmed COVID-19 Disease	Recruiting	682	Confirmed COVID-19	None	Oral NP-120 (Ifenprodil)	Treatment: drug
NCT04394117	Controlled evaLuation of Angiotensin Receptor Blockers for COVID-19 respIraTorY Disease	Recruiting	605	Confirmed COVID-19	None	Oral angiotensin II receptor blockers	Treatment: drug
ACTRN12620000982910	A randomized double-blind placebo-controlled trial of oral ivermectin outpatient treatment, to prevent hospitalisation, of those at high risk for hospitalization due to SARS-CoV-2 (COVID-19)	Not yet recruiting	400	Confirmed COVID-19	Circulatory system disease, respiratory system disease and endocrine disease	Oral ivermectin	Treatment: drug
NCT04439071	Evaluation of the Efficacy and Safety of PTC299 in Hospitalized Subjects With COVID-19 (FITE19)	Recruiting	380	Confirmed COVID-19	None	Oral PTC299	Treatment: drug
NCT03808922	A Phase III Randomized Placebo-Controlled Study to Examine the Efficacy and Safety of DAS181 for the Treatment of Lower Respiratory Tract Parainfluenza Infection in Immunocompromised Subjects	Recruiting	250	Confirmed COVID-19	None	Nebulised DAS181	Treatment: drug

Trial ID	Scientific title	Status	Sample size	Population	Co-morbidity	Drug type	Trial Purpose
ACTRN12620000557932	Therapies to prevent progression of COVID-19, including Hydroxychloroquine, Azithromycin, Zinc, Vitamin D, Vitamin B12 with or without Vitamin C, a multi-centre, international, randomized trial: The International ALLIANCE Study	Recruiting	200	Confirmed COVID-19	None	Intravenous vitamin C (sodium ascorbate)	Treatment: drug
NCT04445467	An Adaptive Randomised Placebo Controlled Phase II Trial of Antivirals for COVID-19 Infection	Recruiting	190	Confirmed COVID-19	None	Oral favipiravir	Treatment: drug
ACTRN12620000731998	Safety and efficacy of a pharmacological strategy using Losartan in hospital patients with COVID-19	Not yet recruiting	36	Confirmed COVID-19	None	Oral losartan	Treatment: drug
ACTRN12620000788976	Safety and efficacy of intranasal delivery of BromAc® (Bromelain & Acetylcysteine) in swab positive SARS-CoV-2 patients – inactivating the COVID-19 virus by cleavage of the spike and other glycoproteins	Not yet recruiting	30	Confirmed COVID-19	None	Intranasal bromelain and acetylcysteine	Treatment: drug
ACTRN12620000470998	Virucidal pilot study of Nasodine® Antiseptic Nasal Spray (povidone-iodine 0.5%) in people with COVID-19 and confirmed nasal shedding of SARS-CoV-2 virus	Not yet recruiting	20	Confirmed COVID-19	None	Intransal Nasodine Antiseptic Spray (povidone-iodine 0.5%)	Prevention: other
NCT04323761	Expanded Access Treatment Protocol: Remdesivir (RDV; GS-5734) for the Treatment of SARS-CoV2 (CoV) Infection	Completed	N/A	Confirmed COVID-19	None	Intravenous remdesivir	Not available

Trial ID	Scientific title	Status	Sample size	Population	Co-morbidity	Drug type	Trial Purpose
ACTRN12620000517976	A randomised controlled trial of Nebulised Heparin in critically ill mechanically ventilated patients with COVID-19 to assess the effect on the duration of mechanical ventilation.	Recruiting	206	Severe COVID-19	None	Nebulised heparin	Treatment: drug
ACTRN12620000447954	Use of therapeutic drug monitoring (TDM) to optimise oral/enteral hydroxychloroquine dosing in critically ill patients with COVID-19	Recruiting	150	Severe COVID-19	None	Oral/enteral hydroxychloroquine	Treatment: drug
ACTRN12620000454976	High-dose intravenous zinc (HDIVZn) as adjunctive therapy in COVID-19 positive critically ill patients: A pilot randomized controlled trial	Recruiting	160	Severe COVID-19	None	Intravenous high dose zinc	Treatment: drug
ACTRN12620000841976	COVID-19 Prevention and Treatment in Cancer; a Sequential Multiple Assignment Randomised Trial; C-SMART study. Arm 3: Effect of selinexor in cancer patients with moderate COVID-19 infection	Not yet recruiting	126	Moderate COVID-19	Neoplasm	Oral selinexor	Treatment: drug
ACTRN12620000478910	Cord Blood Therapy to prevent progression of COVID-19 related pneumonia	Not yet recruiting	24	Moderate COVID-19	None	Intravenous cord blood therapy	Treatment: drug
ACTRN12620000840987	Phase I trial on safety and tolerability of bone-marrow derived mesenchymal stromal cells (MSC) for deteriorating COVID-19 pneumonia	Recruiting	10	Moderate COVID-19	None	Intravenous bone-marrow derived mesenchymal stromal cells	Treatment: drug
ACTRN12620000580976	Tocilizumab for the treatment of COVID-19 in intensive care patients: effect on days free of ventilatory support	Not yet recruiting	150	Severe COVID-19	None	Intravenous tocilizumab	Treatment: drug

Trial ID	Scientific title	Status	Sample size	Population	Co-morbidity	Drug type	Trial Purpose
ACTRN12620000844943	COVID-19 Prevention and Treatment in Cancer; a Sequential Multiple Assignment Randomised Trial; C-SMART study Arm 4: Effect of Lenzilumab in cancer patients with severe COVID-19 infection	Not yet recruiting	72	Severe COVID-19	Neoplasm	Intravenous lenzilumab	Treatment: drug
ACTRN12620000676910	Allogeneic Amniotic Epithelial Cells for the Treatment of COVID-19 related respiratory failure, a pilot feasibility randomised controlled trial	Not yet recruiting	40	Severe COVID-19	None	Intravenous allogeneic amniotic epithelial cells	Treatment: drug
ACTRN12620000612910	A pilot, open-label, randomised controlled clinical trial to investigate early efficacy of CYP-001 in adults admitted to intensive care with COVID-19	Recruiting	24	Severe COVID-19	None	Intravenous allogeneic mesenchymoangioblast-derived mesenchymal stem cells	Treatment: drug

[1] Trial arms were adapted and changes were not reflected through trial registration as of 16th November 2020.

Abbreviations: ARDS, acute respiratory distress syndrome; COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Supplementary Table 2b. Characteristics of all included COVID-19 vaccine trials (n = 10)

Trial ID	Scientific title	Status	Sample size	Population	Co-morbidity	Vaccine type	Trial Purpose
NCT04368988	A 2-Part, Phase 1/2, Randomized, Observer-Blinded Study To Evaluate The Safety And Immunogenicity Of A SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine (SARS-CoV-2 rS) With Or Without MATRIX-M™ Adjuvant In Healthy Subjects	Recruiting	1419	Healthy volunteers	None	Intramuscular SARS-CoV-2 recombinant Spike protein nanoparticle vaccine	Prevention: vaccince
ACTRN12620000817943	A randomized, observer-blind, placebo-controlled, Phase I/II study to evaluate the safety, reactogenicity and immunogenicity of Receptor Binding Domain (RBD) SARS-CoV-2 (COVID-19) Hepatitis B surface antigen (HBsAg) virus like particle (VLP) Vaccine in Healthy Adults	Recruiting	280	Healthy volunteers	None	Intramuscular receptor binding domain SARS-CoV-2 Hepatitis B surface antigen virus like particle vaccine	Treatment: other
NCT04495933	A Phase 1, Randomised, Double-Blind, Placebo-Controlled, Dosage-Escalation, Single Centre Study to Evaluate the Safety and Immunogenicity of an Adjuvanted SARS-CoV-2 Sclamp Protein Subunit Vaccine in Healthy Adults Aged 18 to 55 Years Old and Healthy Older Adults, Aged 56 Years and Over	Recruiting	216	Healthy volunteers	None	Intramuscular adjuvanted SARS-CoV-2 Sclamp protein subunit vaccine	Prevention: vaccince
NCT04405908	A Phase 1, Randomized, Double-blind, Placebo-controlled, First-in-human Study to Evaluate the Safety and Immunogenicity of SCB 2019, a Recombinant SARS-CoV-2 Trimeric S Protein Subunit Vaccine for COVID-19 in Healthy Volunteers	Recruiting	150	Healthy volunteers	None	Intramuscular recombinant SARS-CoV-2 trimeric S protein subunit vaccine	Prevention: vaccince

Trial ID	Scientific title	Status	Sample size	Population	Co-morbidity	Vaccine type	Trial Purpose
ACTRN12620000674932	A Phase 1 Randomised, Double-Blind, Placebo-Controlled, Dosage-Escalation, Single Centre Study To Evaluate The Safety And Immunogenicity Of An Adjuvanted SARS-CoV-2 Sclamp Protein Subunit Vaccine (COVID-19 vaccine) In Healthy Adults Aged 18 To 55 Years Old	Recruiting	120	Healthy volunteers	None	Intramuscular adjuvanted SARS-CoV-2 Sclamp protein subunit vaccine	Prevention: vaccince
NCT04453852	A Randomised, Controlled, Phase 1 Study to Evaluate the Safety and Immunogenicity of a Candidate Adjuvanted Recombinant Protein SARS-COV-2 Vaccine in Healthy Adult Subjects	Recruiting	40	Healthy volunteers	None	Intramuscular adjuvanted recombinant protein SARS-COV-2 vaccine	Prevention: vaccince
NCT04334980	A Phase 1, Randomized, Observer-Blind, Placebo-Controlled Trial to Evaluate the Safety, Tolerability and Immunogenicity of the bacTRL-Spike Oral Candidate Vaccine for the Prevention of COVID-19 in Healthy Adults	Not yet recruiting	12	Healthy volunteers	None	Oral bacTRL-Spike vaccine	Prevention: vaccince
ACTRN12620000707965	A Multicenter, Phase III, Double-Blind, Randomized, Placebo-Controlled Study to Evaluate the Efficacy of the recombinant BCG VPM1002 on the Incidence or Disease Severity of SARS-COV-2/COVID-19 Among High-Risk Participants in Australia	Withdrawn (commercial reasons)	3468	Individuals at high-risk of poor outcomes	Circulatory system disease, respiratory system disease and endocrine disease	Intramuscular recombinant Bacillus Calmette–Guérin (BCG) vaccine VPM1002	Treatment: other
NCT04333732	An International, Multi-site, Bayesian Platform Adaptive, Randomized, Placebo-controlled Trial Assessing the Effectiveness of Candidate Agents in Mitigating COVID-19 Disease in Healthcare Workers	Not yet recruiting	30000	Healthcare professionals	None	Adaptive design [1]	Prevention: vaccince
NCT04327206	BCG Vaccination to Reduce the Impact of COVID-19 in Healthcare Workers Following Coronavirus Exposure (BRACE) Trial	Recruiting	10078	Healthcare professionals	None	Intramuscular BCG vaccine	Prevention: vaccince

[1] Trials with adaptive design are subject to change and have been grouped as per information current on the 16th of November 2020.
Abbreviations: COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Supplementary Table 2c. Characteristics of all other included COVID-19 trials (n = 12)

Trial ID	Scientific title	Recruitment status	Sample size	Population	Co-morbidity	Intervention type	Trial Purpose
ACTRN12620000477921	The use of a simplified negative pressure cuirass style ventilator under COVID-19 pandemic conditions in support of critically overwhelmed healthcare systems	Completed	1	Healthy volunteers	None	Simplified negative pressure cuirass style ventilator	Treatment: other
ACTRN12620000688987	Comparing the user seal check and fit test between two types of N95 respirators in anaesthetic staff members - the Halyard N95 Particulate Filter Respirators and the ProShield® N-95 masks	Completed	80	Healthcare professional	None	Halyard N95 Particulate Filter Respirators and the ProShield® N-95 masks	Treatment: other
ACTRN12620000579998	Simulation time taken amongst consultant anaesthetists to perform spinal anaesthesia or general anaesthesia for COVID-19 patients requiring an emergency category 1 caesarean delivery	Not yet recruiting	10	Healthcare professional	None	Anaesthesia	Other
ACTRN12620000640909	A phase II, open label non-randomised clinical trial of the safety and efficacy of the CovidCare app to support self-monitoring for COVID-19 symptoms in self-isolation and to determine the impacts on mental health	Not yet recruiting	200	Exposure to COVID-19	None	CovidCare app	Treatment: other
ACTRN12620000698976	Does a Health Package of exercise and advice on anxiety management and nutrition improve outcomes and experiences of patients with COVID-19 isolated at home or Special Health Accommodation under the care of Royal Prince Alfred (RPA) Virtual Hospital and those without COVID-19 quarantined in Sydney Local Health District Special Health Accommodation?: a pilot trial	Recruiting	40	Exposure to COVID-19	None	Exercise and advice on anxiety management and nutrition	Prevention: other

Trial ID	Scientific title	Recruitment status	Sample size	Population	Co-morbidity	Intervention type	Trial Purpose
ACTRN12620000472976	Adapting the Decathlon Group Easybreathe® snorkelling face mask for the safer administration of oxygen and/or continuous positive airway pressure and in the intra/interhospital transportation of patients with proven or suspected COVID 19 infection	Not yet recruiting	100	Suspected/ confirmed COVID-19	None	Decathlon Group Easybreathe® snorkelling face mask ventilator	Treatment: other
ACTRN12620000524998	ReCOVER (Remote COVID-19 Evaluation and Response): a prospective non-randomised controlled trial to evaluate the effect of a novel smartphone application-centric model of care for the remote monitoring of COVID-19 patients in the community, on avoidable hospital presentations	Not yet recruiting	2000	Confirmed COVID-19	None	Remote monitoring smartphone application and care model	Treatment: other
ACTRN12620000566932	BEAT COVID-19: A Bayesian adaptive randomised controlled trial platform to evaluate the efficacy of interventions for high risk older patients with COVID-19 in reducing the risk of hospital admission or death	Not yet recruiting	400	Confirmed COVID-19	Circulatory system disease, respiratory system disease, nervous system disease, immune system disease, endocrine disease and neoplasm	Treatments or interventions [1]	Treatment: other
ACTRN12620000443998	Home telerehabilitation for people with COVID-19: Implementing telehealth approaches to care and its effect on reintegration into the community	Not yet recruiting	58	Confirmed COVID-19	None	Home tele rehabilitation	Treatment: other

Trial ID	Scientific title	Recruitment status	Sample size	Population	Co-morbidity	Intervention type	Trial Purpose
ACTRN 12620000635965	Open label, prospective study for the Biofourmis Everion armband telemonitoring solution for patients during COVID-19 home isolation within South West Sydney to assess the feasibility and suitability of the Everion armband device in the telemonitoring of COVID-19 high risk patients under home isolation period	Not yet recruiting	50	Confirmed COVID-19	None	Biofourmis Everion armband telemonitoring solution	Prevention: other
ACTRN12620000500954	A reusable personalised ventilation hood for care of patients with suspected or confirmed COVID-19 in the intensive care, emergency and respiratory healthcare settings: A phase 1 safety study of a new device (McMonty)	Not yet recruiting	20	Confirmed COVID-19	None	Reusable personalised ventilation hood	Prevention: other
ACTRN12620000740998	A Randomised Controlled Trial of Early Prone Positioning to Improve Oxygenation in Non-Intubated Adults Admitted to Intensive Care with COVID-19	Not yet recruiting	20	Confirmed COVID-19	None	Early prone positioning	Treatment: other

[1] Trials with adaptive design are subject to change and have been grouped as per information current on the 16th of November 2020.
Abbreviations: COVID-19, coronavirus disease 2019.

Supplementary Table 3. Characteristics of COVID-19 related trials (n=12)

Trial ID [1]	Scientific title	Status	Sample size [2]	Population	Health area	Health area specifics	Intervention details
ACTRN12620000975998	Feasibility and acceptability of a volunteer-peer telephone support programme for individuals diagnosed with COVID-19	Not yet recruiting	100	Persons diagnosed with COVID or in close contact with COVID who accessed healthcare by Northern Health Victoria	Mental health	Depression, loneliness and social isolation	Weekly phone calls (20-40 min) from volunteers (supported by psychologists) for a 12-week period, social in nature. No control, all participants tracked over time.
ACTRN12620000811909p	Randomised Controlled Trial of Positive Mood Training versus Enhanced Treatment as Usual on Anxiety and Depression in People Distressed by COVID-19	Not yet recruiting	240	Persons suffering anxiety and depression	Mental health	Depression and anxiety	Random allocation to Positive Mood Training (weekly 60 min video-conference sessions for 7 weeks with psychologist) or Enhanced Treatment as Usual (provided a self-guided manual).
ACTRN12620000787987p	Randomised Controlled Trial of Problem Management Plus versus Enhanced Treatment as Usual on Anxiety and Depression in People Distressed by Financial Problems Due to COVID-19	Not yet recruiting	206	Persons suffering psychological distress	Mental health	Depression and anxiety	Random allocation to Problem Management Plus program (weekly 60 min video-conference sessions for 7 weeks with psychologist) or Enhanced Treatment as Usual (access to a self-guided problem management plus manual).
ACTRN12620000779976	A pragmatic study to disseminate low intensity, evidence supported Cognitive behaviour therapy and the effect on anxiety and depression in adults during the COVID-19 pandemic	Recruiting	100	Individuals accessing mental health services	Mental health	Depression and anxiety	Participants are provided a self-help guide on Cognitive Behaviour therapy upon completion of registration (immediate group) or one week after registration and following post-intervention questionnaire completion (waitlist group).
ACTRN12620000636954p	COACHING FOR COVID-19: A Pilot Study Investigating the Effectiveness of Coaching on Psychological Outcomes in Hospital-Based Senior Doctors	Not yet recruiting	35	Senior doctors employed by Liverpool Hospital	Mental health	Depression, anxiety, other mental health and Healthcare professionals	Doctors are matched with a coach and meet via Zoom (1 x 30 min intro, 1 x 60 min first session, followed by 5 x 30 min sessions at 3-week intervals) where psychological stress will be monitored throughout.
ACTRN12620000571976	Evaluation of Shift, a smartphone application for New South Wales Junior Medical Officers, on depression and anxiety during the COVID-19 epidemic.	Completed	75	Junior medical officers in NSW	Mental health	Depression, anxiety and healthcare professionals	Participants are all provided with access to the 'Shift' app to address pandemic-related concerns. Participants can use 2-5 activities (of a total 51) per week. Pre- and post-assessment is made.
ACTRN12620000555954	Randomised controlled trial of an app-based intervention, Anchored, to support the mental health of Australians recently unemployed due to COVID-19.	Completed	492	Persons who are unemployed as a result of COVID-19 and experiencing	Mental health	Anxiety, depression, suicide and unemployment	Random allocation to the 'Anchored' smartphone app (5-10 min completed daily) or given access to a psycho-

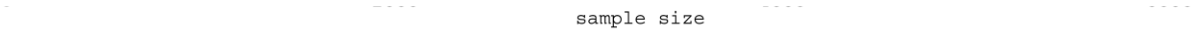
				symptomatic depression			educational online resources for a 30-day period.
ACTRN12620000468921p	Randomised Controlled Trial of Problem Management Plus versus Enhanced Treatment as Usual on Anxiety and Depression in People Distressed by Covid 19	Not yet recruiting	140	Persons suffering psychological distress	Mental health	Depression and anxiety	Random allocation to Problem Management Plus program (weekly 60 min video-conference sessions for 6 weeks with psychologist) or Enhanced Treatment as Usual (access to a website outlining evidence-based mindfulness strategies).
NCT04602312	Online RCT Comparing the Effects of Mindfulness, Sham Mindfulness and Book Listening Control on Coronavirus-related Catastrophizing in Adults	Recruiting	624	Healthy individuals	Mental health	Anxiety, stress and catastrophising	Random allocation to mindfulness meditation, specific sham mindfulness meditation, general sham mindfulness meditation or book listening control via 1 x 20 min online audio training.
ACTRN12620000448943	Expressive Writing To Combat Distress Associated With The COVID-19 Pandemic In People With Inflammatory Bowel Disease	Recruiting	154	Person diagnosed with inflammatory bowel disease and suffering mild distress	Mental health and gastrointestinal disease	Depression, anxiety and inflammatory bowel disease	Random allocation to an expressive/gratitude writing program (4 x 30 min sessions in one week writing about their inflammatory bowel disease based on an evidence based writing program) or an active control (4 x 30 min sessions in one week writing about trivial topics). Both sessions conducted by researcher with psychology degree.
ACTRN12620000492954p	Feasibility of a Facebook delivered physical activity focused group lifestyle intervention for older adults during the COVID-19 pandemic	Not yet recruiting	20	Healthy individuals >60 years living alone	Mental health and physical activity	Depression, physical inactivity and older adults	Participants receive weekly information and contribute to conversations on topics relating to physical activity for a 6-week period through a private Facebook group, delivered by an exercise physiologist and dietitian. Participants can also join 20-30 min Zoom calls organised twice each week.
ACTRN12620000860965	A randomised controlled trial on the effect of a smart device enabled monitoring system on management of heart failure among patients with pre-existing left ventricular dysfunction during COVID-19 isolation	Not yet recruiting	400	Persons with left ventricular dysfunction or heart failure who do not have impaired cognitive function	Cardiovascular disease	Heart failure, and cardiac rehabilitation	Random allocation of access to a smartphone app, in addition to standard care to manage cardiac rehabilitation at home. Daily reporting of blood pressure, medication adherence, task completion, stress, heart rate, goals and patient reported outcomes. Entries are reviewed by patient's clinician.

[1] Provisional trials are indicated with a 'p', and have been submitted but not yet approved by the ANZCTR.

[2] Sample size represents the target sample size as indicated on the trial record.

Abbreviations: COVID-19, coronavirus disease 2019.

Supplementary Figure 1. Power calculations to detect mortality for hospitalised COVID-19 patients



*indicative mortality rates have been extracted (2).
Abbreviations: COVID-19, coronavirus disease 2019; n, number.

References

1. Tong A, Elliott JH, Azevedo LC, Baumgart A, Bersten A, Cervantes L, et al. Core outcomes set for trials in people with coronavirus disease 2019. *J Crit Care Med*. 2020; 48: 1622-35. 10.1097/CCM.0000000000004585.
2. Dennis JM, McGovern AP, Vollmer SJ, Mateen BA. Improving Survival of Critical Care Patients With Coronavirus Disease 2019 in England: A National Cohort Study, March to June 2020. *J Crit Care Med*. 2020; 49: 209-14. 10.1097/ccm.0000000000004747.